THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY
CHENNAI -600032.

A PROSPECTIVE ANALYTICAL STUDY ON CT GUIDED FRAMELESS STEREOTACTIC BRAIN BIOPSY

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CERTIFICATE

This is to certify that this dissertation entitled **"A PROSPECTIVE ANALYTICAL STUDY ON CT GUIDED FRAMELESS STEREOTACTIC BRAIN BIOPSY"** submitted by **Dr. S. SIVA SUBRAMANYAM**, appearing for **M.Ch (Neurosurgery)** degree examination in August 2013 is a original bonafide record of work done from August 2010 to February 2013 by him under my guidance and supervision in partial fulfillment of requirement of the Tamil Nadu Dr.M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

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DECLARATION

I, Dr. S. SIVA SUBRAMANYAM, solemnly declare that this dissertation **"A PROSPECTIVE ANALYTICAL STUDY ON CT GUIDED FRAMELESS STEREOTACTIC BRAIN BIOPSY"** was done by me at the Institute of Neurology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai under the guidance and supervision of the Professor of Neurosurgery, Institute of Neurology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3, between 2010 and 2013.

This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai-600032 in partial fulfilment of the University requirements for the award of the degree of M.Ch., Neurosurgery.

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(_____)

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TABLE OF CONTENTS

ABBREVIATIONS USED

A 1 – astrocytoma grade I
A 2 – astrocytoma grade II
A 3 – astrocytoma grade III
A 4 – astrocytoma grade IV
BRW – Brown-Roberts-Wells
CT – computerized tomography
CTSP – CapeTown Stereotactic Pointer
CRW – Cosman-Roberts-Wells
CSF – cerebrospinal fluid
HPE – histopathological examination
ICH – intra cerebral hemorrhage
ICP – intra cranial pressure
MRI – magnetic resonance imaging
OT – operation theatre
SAH – sub arachnoid hemorrhage
STB – stereotactic biopsy
US – ultrasound

INTRODUCTION

INTRODUCTION

Inspite of the vast improvements in neuroradiological modalities in recent times, pathological diagnosis is essential for the diagnosis and planning of treatment of any brain pathology. Obtaining samples for histopathological examination (HPE) by craniotomy is sometimes fraught with risks and complications unique to open methods. Stereotactic methods are helpful in achieving a reliable and accurate sampling of intracranial lesions, which are superior to open methods in terms of safety and to free hand methods in morbidity, mortality, and diagnostic yield[7]. Stereotactic biopsy (STB) is a method tested in time for accurate sampling of brain lesions. The uses of STB in brain pathology are almost limitless. It is not limited by the site and location of the lesion, condition of the patient, and size of the lesion.The advantages of frameless apparatus over frame based ones are: (1) only fiducials or the base containing them need to be attached to skull, (2) lesions at sites that are limited by frame like posterior fossa are also made accessible, (3) it does not pose a hindrance to the surgical field, (4) does not limit the mobility of the patient, (5) maneuvering the apparatus during surgery is easy, and (6) administering general anesthesia is not obstructed. The accuracy and safety of the frameless biopsy are comparable with that of frame based ones.

Therefore this study on frameless stereotactic brain biopsy method was conducted.

AIMS AND OBJECTIVES

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1. To collect and analyze the Demographic Data of the patients undergoing stereotactic biopsy
2. To analyze the Indications, Complications and Yield of biopsy in frameless stereotaxy
3. To evaluate the ease and feasibility of stereotactic biopsy
4. To enable the neurologists and neurosurgeons to understand and correlate the varied clinical manifestations.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Brief history

Neurosurgeons in late 19th century and early 20th century relied exclusively on anatomical knowledge of brain and clinical findings to plan their operative approaches. D. N. Zernov, in 1889, was the first person to use an instrument for locating brain structures, who designed an apparatus that could be fixed to the head and then be identified on a map which showed the average positions of cranial structures. In 1906 , a method of localizing brain structures in animals was described by Victor Horsley and Robert Clarke[1]with a frame based on a Cartesian coordinate system.

In 1947 the first human stereotactic system, termed the encephalotome, was introduced by Spiegel and Wycis[2,3]. They combined x-ray technology with ventriculography, a method in which air or contrast material is introduced into the ventricles to have clear images of X-rays. Then targeting of an instrument toward a particular neural structure based on information obtained earlier was done. Lars Leksell[4] in the same time utilized polar coordinate system in the instrumentation for STB. With the introduction of CT in 1973 and MRI in 1980, frame-based stereotactic guidance took a firm place in the conduct of neurosurgical operations. The examples are Brown-Roberts-Wells (BRW) and Cosman-Roberts-Wells (CRW)[5,6] systems.

Frameless stereotactic biopsy

Frameless stereotaxy is based on creating a mathematical relationship between images from CT or MRI and physical space. The relationship between image space and the actual physical space of cranium is defined in 3 dimensional variables and thus a map is formed for navigating through the physical space. This is called registration. Interactive localizing device is used to define a stable coordinate system between the image and the physical space.

Cape Town Stereotactic Pointer (CTSP)

Cape Town Stereotactic Pointer (CTSP) is used in this study. It utilizes stereophotogrammetric principles to locate any unique point in space with the help of images of CT or MRI as measuring medium.

Scopes

The uses of STB are varied. It is useful in both diagnostic instrumentation and therapeutic utilities. It can be used to precisely sample from lesions, both neoplastic and non-neoplastic, abscesses, intraaxial and extraaxial lesions, lesions located in deeper structures of brain, and lesions located in eloquent regions. It may also be utilized to drain abscesses, thrombolyse and drain hematomas, place tubes like Ommaya tubes etc.

As it utilizes a biopsy needle of small diameter it causes minimal distortion or damage to brain structures. As the tract of needle can also be predetermined it can be introduced along a path avoiding eloquent regions. As it requires only a burr hole to introduce the biopsy needle, the risk of infection is also minimal.

The procedure requires only a burr hole and can be done under local anesthesia. The invasiveness of the procedure is kept minimal and to the last. The procedural time is in minutes and the patient can return to normalcy as soon as he/she is out of the operation suite. Even if done under general anesthesia, this procedure is simple and non-restricting.

Limitations

As with every principle and utility this method also has its own limitations. The calculation of the location, though may be simple, is not free from errors. This can adversely affect the yield of biopsy and management. As it relies only on images it is not a direct sampling method of biopsy.

The sample volume is understandably smaller than direct methods. This may affect the accuracy and grading of lesions. The smaller sample volume may not always allow intraprocedural frozen section or squash study.

As there is no way to detect vessels along the track of needle it may be difficult to avoid them. Noticeably hemorrhage is the most common and adverse complication attributed for this method by researchers.

The image may not always represent the actual physical corpus due to shift of brain as in case of change in volume due to anesthetic drugs, or anti edema measures started before the procedure, or loss of cerebrospinal fluid (CSF) during durotomy.

Complications

Hemorrhage is reported to be the major complication associated with this procedure. It may adversely affect the outcome of the patient, causing even death. It is also reported to lower the yield and accuracy of sample obtained.

Another complication possibly associated with STB is infection. It is possible in cases of abscess location for obvious reasons. But in STB for non-infectious causes, this complication is minimal to the point of nonexistance.

The possibility of seeding of tumor cells along the track of needle cannot be ruled out. There are few cases reported to have track site metastasis in high grade gliomas [7,8,9].

A case report is on the complication of pneumocephalus following STB. This also should be considered in this setup[10].

But the reported complications are few and less than that of open procedures and the safety profile of this procedure have been tested to a large extent.

Stereotactic biopsy is a minimally invasive procedure, where the biopsy is directed along the specified path predetermined by images obtained by CT or MRI. Its accuracy and safety profiles are attested by various studies over many eras. According to various studies the samples obtained for histopathology by stereotactic biopsy is accurate enough when compared with open biopsies.

The comparison of free hand technique versus stereotactic biopsy

Lee T et al[11] in comparing 2 groups of patients who underwent STB and freehand burr hole biopsy (153 and 217 patients respectively), found that the

rates of complications and death of STB were significantly lower (2.6 and 1.3% respectively) while compared with freehand (7.8 and 7.8% respectively) and the diagnostic yields were 92.1 and 64.9%, for each method respectively.

The comparison of open resection and STB.

While comparing the results of STB and resected specimen *Chandrasoma et al*[12] found that the yield was 28/30 and the accuracy was 19/30. Correlation was not perfect in 9/30 cases. 2 of 30 cases were inaccurate. One was reported as necrotic tissue while on resection found to be glioblastoma and the other was directed towards inflammatory region and was reported as that while the resected specimen showed germinoma.

In their study, *Feiden W et al*[13] compared the histological findings in biopsy cylinders obtained from STB and resected tumor specimen. Their study group consisted of 47 patients. Leksell CT frame was used in performing STB and a spiral needle was used in taking samples. Usually, 3 to 4 biopsy specimens were taken along the track placed through the whole lesion and its margins according to the CT imaging. In 42 cases (89%), the histological results in biopsy and resection/autopsy tissue were identical. In 3 patients with a diagnosis of brain lymphoma and low grade glioma on the basis of the surgical specimens, stereotactic biopsy revealed only unspecific reactive tissue changes. In two cases of the early part of the study, sampling errors occurred. Their conclusion was STB correctly diagnosed the lesion in most of the cases as compared with resected specimen.

Grunert P et al[14] in their study compared the intraoperative findings from STB with final results. They also analyzed 41 cases with resected specimen or postmortem results. There was discrepancy in 1 patient regarding diagnosis and in 3 cases on grading. The mortality was 1 percent and morbidity of 3 percent. They concluded that STB was safe even in gangliocapsular, brainstem and pontine regions.

Frameless stereotaxy differs from Frame-Based ones in that they attach fiducials to skull or scalp and with images of CT or MRI, plan a "map" towards the lesion and direct the instrument to get samples. They are comparable with frame based ones in terms of safety and diagnostic yield. Various studies have compared both methods and have found no significant differences between the two. The frameless methods offer advantages of ease, patient mobility, and ease of wielding the biopsy and anesthetic instruments.

Frame-based and frameless biopsy

Jain D et al[15] compared the reliability of diagnosis on CT guided, frame based, frameless and ultrasound (US)-guided methods of biopsies. This study was on 130 cases over a period of 10 years in a retrospective method. They were able to establish a definite pathological diagnosis in 109 cases (80.2%). 95, 15 and 20 patients underwent frame-based, frameless stereotactic and US-guided biopsies respectively. Frameless image-guided STB yielded a better diagnosis than CT guided frame based STB and US-guided biopsy [87% (13/15)] comparatively.

Dammers et al[16] compared frame based and frameless STB methods found that both methods yielded a diagnosis of 89.4%. They have analyzed retrospectively on 391 cases (227 frame-based and 164 frameless) over a period of 10 years. Postoperative morbidity was noted in 12.1% cases, which included 15 cases of bleeding (3.8%). No difference existed in complication rates when comparing both procedures. Biopsy-related deaths increased with perioperative complications and deep-seated pathologies. Symptomatic bleeding caused death among 1.5% of all patients.

The common indication for biopsy is a deep-seated lesion.

Deep seated lesions

Kelly et al[17] in a study on thalamic gliomas by STB which included 72 patients who had histologically verified thalamic astrocytomas, have concluded that though STB was accurate in diagnosing thalamic astrocytomas, patients who have significant mass effect may benefit from stereotactic resection.

METHODS TO IMPROVE THE YIELD

Intraoperative biopsy

Shooman D et al[18] in a prospective study analyzed all patients who underwent CT guided STB over a period of more than 2 years and concluded that as the positive results obtained from STB were maximal, intraprocedural pathological examination may not increase the positive yield any further.

O'Neill KS et al[19] had stressed the need for peroperative biopsy in reducing the need for serial interventions. Peroperative cytology was assessed in a five year

study of CT guided STB of space occupying lesions of brain. 259 STB were performed in 245 cases. 24 cases had benign lesions (9.8%). In the initial 142 cases intraoperative histopathological diagnosis was not available and the yield was 86.6%. In the subsequent 103 cases intraoperative samples were available which caused an improvement in the yield to 94.2% and reduction in the need for second biopsy from 7 to nil.

Site of biopsy

Greene et al[20] in their study on 27 cases, undergoing twenty nine CT guided STB for malignant astrocytomas analyzed the site of biopsy and the yield. Biopsies were obtained at 3 places, from the central hypodensity, contrast enhancing margin, and hypodense periphery. They found that the yield in the central hypodensity or contrast enhancing margin was higher. They concluded that for improved diagnostic yield serial STB needed to be directed towards the central hypodensity and contrast enhancing margin.

Yield and multiple biopsies

Fritsch et al[21], in their study had 65 consecutive biopsies analyzed on STB for intraaxial lesions. A side cutting biopsy needle was used in this study. They attributed the high diagnostic yield to the high number of biopsies taken per lesion. They have noted no increase in complication rates though with increased sampling numbers.

Side cutting needle

Hirschfeld A et al [22] reported in their study the superiority of side cutting needle over cup forceps in sampling.

The study of stereotaxy has evolved for more than a century from those relying on x rays and air contrast in ventricles to CT and MRI and MR spectroscopic images, and from rigid frames to frameless ones. The complication rates have shown a definite decrease over time.

Age and Gender as predictive factors for yield

Ferreira MP et al[23] analyzed various predictive factors on diagnostic yield. 170 cases undergoing CT guided stereotactic biopsy over a period of 12 years were analyzed retrospectively for age, sex, pathological diagnosis, volume of lesion, location, complications for predictive factors in the diagnostic yield. 157 out of 170 cases were diagnosed correctly of the lesion. The most frequent histopathological diagnosis was high grade glioma (45), low grade glioma (31), nonspecific inflammatory lesions (19), secondaries (10), and lymphoma (10). The common locations were frontal (n = 42), gangliocapsular (n = 40), parietal (n = 27) and frontoparietal region (n = 9). Rate of morbidity was 2.9% (5/170). 2 patients died (1.2%). They concluded that age was positively associated with yield, and female gender had an impact in a negative way. No other factor was significant.

CT Findings and yield

Non diagnostic biopsies in CT guided STB were analyzed by *Ranjan A et al*[24] in 407 patients. The results were classified as negative, inconclusive, and positive. 19 (4.7%) were negative and ten (2.4%) were not conclusive. Based on CT features the suspicious mass lesions (n=390) were categorized into 4 groups: (1) non enhancing hypodense lesions; (2) non enhancing iso dense lesions; (3) peripheral enhancing lesions; and (4) variably enhancing lesions. There was no statistical significance between the different groups in the yield rate, although non enhancing hypodense lesions had negative biopsies as compared with other groups (p = 0.06). They concluded that the yield in a STB was not dependent on the characteristics on CT images.

COMPLICATIONS

In a study, *Ali Z et al*[25] reviewed the complications occurring in peroperative and post-operative period during frameless stereotaxy from January 2003 to July 2007. The study was conducted on 78 patients undergoing STB. Intraoperative adverse reactions noted were intraoperative edema (*n* = 3), convulsions (*n* = 3), inability to extubate (*n* = 4), and neurological deficits (*n* = 6). There was no shock, adverse change in blood pressure or pulse rate noted.

In analyzing the complications following STB of intraaxial brain lesions by CT-guidance, *Bernstein et al*[26] concluded that the complication rates were 6.3% and mortality rate was 1.7%. They have analyzed 300 cases that underwent STB, for complications. 2 among the 5 died had intracranial hemorrhage. All who died

were due to increased intra cranial pressure (ICP): 1 had sub arachnoid hemorrhage (SAH), 1 had intra cerebral hemorrhage (ICH), and 3 from increased edema without hemorrhage. All who died without hemorrhage had marked ICP during the time of the procedure. They were all diagnosed with glioblastoma.

Chen et al[27] in their single center study which was conducted to analyze the complications concluded that in STB procedures the overall diagnostic yield of was 90.64%. Morbidity was seen among 7.36% of the patients, among which symptomatic intracranial bleeding occurred in 4.35%. In this study the observed death rate was 1.34%. They found only liver cirrhosis patients had increased risk of bleeding.

Sawin PD et al[28] undertook a study to investigate for variables that may be contributing to the rise of complications from STB. They had a review of 225 consecutive CT assisted STB. They found out that the use of antiplatelet agents, corticosteroids, deepseated lesions, high grade gliomas, and an increased number of attempts at biopsy were all had association with complications ($p < 0.05$). Other factors were not significantly associated with complications included age, sex, comorbidities, HIV status etc. Factors associated with increased operative risk were site of the lesion, pathology, administration of steroids, antiplatelet therapy and surgery.

PREDICTORS OF HEMORRHAGE

The value of preoperative variables in predicting the complications related to the procedure was assessed by *McGirt MJ et al*[29] in their study on 270 patients the records of whom were analyzed retrospectively and found that pathologies located in basal ganglia and thalamus and diabetic status had increased association with complications related to STB. Blood sugar levels on the day of STB had a predicting value in patients with diabetes. Epileptic disorders did not predispose to STB associated convulsions.

Transient and permanent STB-related complication was noted in 23 and 13 (9% & 5%) cases, respectively. In twenty five patients there was bleeding at the biopsy site (9%) and 10 (4%) among them had clinical symptoms. Blood sugar levels, lesions located in thalamus, and basal ganglia were associated with complications. In patients with diabetes mellitus, plasma sugar level > 200 mg/dl on the day of procedure had a positive predictive value of 100% and levels < 200 mg/dl had a 95% negative predictive value for STB-related complications.

Post procedural CT

Field M et al[30]*,* in their prospectively conducted study, tried to determine the rate of hemorrhage after STB by performing immediate CT brain. They analyzed prospective factors influencing hemorrhage and the yield of biopsy. 500 consecutive patients undergoing STB underwent immediate CT scanning. In 8% (40) hemorrhage was detected on CT scans. 6 patients had neurological

deficits (1.2%) and 1 died (0.2%). Though there was no hemorrhage detected on immediate CT scan, symptomatic deficits were present in 2 patients (0.4%) later on. Both had large intracerebral hemorrhages on repeat CT scan. The only significant factor associated with hemorrhage was a platelet count <150 000/mm^3. Pineal lesions were also shown to have a significant association with hemorrhage measuring > 5 mm in diameter. As the number of biopsy samples increased, the specimens obtained without definite results also increased. Younger patient age also correlated with negative biopsy.

Deep seated lesions and Grade 4 astrocytoma

Kongkham PN et al[31] studied the complications and the clinical variables in 614 cases undergoing frame based STB over a period of 20 years in which STB was done for diagnostic purposes. Complication and death rates were 6.9% and 1.3% (43/622, 8/622), respectively. The risk of intracranial hemorrhage was 4.8% and the risk of developing permanent or transient deficits were 1.5 & 2.9 % (9/622,18/622) respectively. Complication rate increased with STB of deeper lesions and biopsy of Grade 4 astrocytoma had association with procedure related deaths.

Brain stem location as predicting factor

Grossman R et al[32] in their study on hemorrhagic complications in 355 consecutive patients undergoing STB reported 25 cases (7%) had intracerebral bleeding, but 3.4% of cases had no altered course in the recovery. Morbidity was symptomatic in 13 (3.6%) and 2 died (0.6%). Brain stem lesions had

complication rates higher than that of other sites. Symptoms occurred acutely in 7 cases, and in 6 it was delayed, developing after hours or sometimes after days.

Abscess

The success rate in diagnosing brain abscess with stereotaxy was also high. *Barlas et al*[33] published in their study on 23 cases of brain abscess diagnosed with stereotaxy, that all were aspirated and diagnosed. The complications were minimal and reversible.

Ersahin M et al[34] in their study on thirteen patients with intracranial masses suspected with tuberculoma who underwent stereotactic procedures for establishing a tissue diagnosis, found the success rate was 92%. In 6 of 13 patients, stereotactic microsurgical excision was performed, and STB in others. A diagnosis of tuberculoma was arrived at in twelve among the thirteen cases (92%). Seizure control was achieved in all patients admitted with a history of seizures. There was no death directly due to the procedure, and no one suffered permanent disability and most procedures were uneventful. The response to antituberculous therapy was successful.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design

The study was undertaken at The Department of Neurosurgery, Institute of Neurology, affiliated to Madras Medical College and Government General Hospital, Chennai. The Barnard Institute of RadioDiagnosis at Madras Medical College has five CT installations and one MRI installation. The Department of NeuroPathology affiliated to our Institute is dedicated exclusively for the analysis and interpretation of specimens related to brain pathologies. Their services were utilized for this study.

This was a prospective study analyzing patients undergoing CT guided stereotactic biopsy between Aug 2010 and Mar 2013. Over a period of 2 years and 3 months 35 patients participated in the study. Patients were selected who were conforming to the selection criteria for the study and got informed written consent to participate in the study.

Patients with brain lesions deemed not amenable for complete resection, lesions in which resection may be associated with complications and lesions that required a biopsy to confirm its nature, deep seated lesions, lesions in eloquent regions, small lesions, and patients who were not willing for open biopsy **were included** in the study. Patients in whom medical conditions preclude a craniotomy or resection **were included** in the study.

Patients with disorders of coagulation and deranged coagulation profiles, extraaxial lesions, and vascular lesions **were excluded** from the study.

METHODOLOGY

Instrument

Cape Town Stereotactic Pointer was used in the study for instrumentation in the procedure of stereotactic biopsy. A side cutting needle was used for sampling out specimen.

Radiology

Radiological images were got from 2 of the 5 CT installations [(1)Asteion VF, Single slice axial CT, Toshiba Inc., Japan, (2) Asteion Super 4, 4 slice CT, Toshiba Inc., Japan] of our hospital.

Apparatus

CapeTown Stereotactic Pointer was used for all procedures of stereotactic biopsy. It works on the principle of stereophotogrammetry and uses CT or MRI images for measurements[35]. This study utilized the CT images and fiducial base for CT images for measurement purposes. It consists of a phantom frame(fig 5), on which the phantom coordinates are extrapolated, a tripod, to be mounted on the CT frame(fig 6), a CT frame which lodges the fiducials in 3 legs, a biopsy mount, to hold the biopsy needle, a biopsy needle (fig 7) to reach and procure tissue samples.

The biopsy needle is a side cutting double hollow cylinder which is blunt at its end and uniform in its diameter. This design causes minimal tissue displacement

during needling, and accurately samples the tissue. It consists of two tubes. The outer tube is hollow and functions as a sheath with rectangular shaped defect at its terminal end for the tissue to lodge in. The inner tube is also a hollow cylinder snuggly fitting inside the outer sheath, which can be rotated inside the sheath to cut the tissue sample lodged inside (fig 10, 11 ,12).

Procedure

From the radiological images obtained earlier, the site, location, depth from surface of the lesion and relation of it to all neighboring normal structures of the brain especially the vessels was determined. Scalp was scrubbed and painted with 10% povidone iodine solution and left for 3 minutes to dry. Lignocaine infiltration was done in appropriate dose at the sites of fixing the frame. The CT frame was fixed with nylon stitches over scalp nearest to the lesion, commonly over the frontal, parietal or occipital eminences. It lodges the fiducials for identification on the CT images (fig 1). The patient was shifted to CT suite. CT plain axial images were taken in 3 mm cuts with the frame. The Cartesian coordinates of the 3 fiducial markers and that of the point on tumor where biopsy was to be taken were obtained with respect to a reference frame placed on the images from CT (fig 14,15,16,17). The central point or the enhancing portion of the tumor was usually selected for biopsy. The Cartesian coordinates were fed to the CTSP software and phantom coordinates were calculated from it.

The patient was then shifted to OT room. On the phantom frame the calculated phantom coordinates were extrapolated and the trajectory, depth and site of entry were derived (fig 7). Under local anesthesia or general anesthesia patient was laid supine comfortably on the table positioning the frame at the top, and the site was painted and draped again (fig 8). 3% glutaraldehyde or 10% povidone iodine was used for painting the site. The site of burr hole was estimated, and made on skull (fig 9). Dura was opened with unipolar cautery and pia opened with bipolar cautery. Side cutting biopsy needle was then inserted along the previously calculated path to the tumor and multiple cylinders of tissue specimens procured. A minimum of 4 biopsies were taken for investigation (fig 13). After securing hemostasis the frame was removed and site closed in layers, galea with vicryl stitches and scalp with nylon stitches. After reversing the patient out of anesthesia, the patient is taken to CT room, and a repeat non contrast CT brain was taken and looked for any new changes like edema, shift, tumor bleed, or hematoma along the track or elsewhere. The trajectory was also looked for, which would be seen as a speck of air or a thin track of hematoma (fig 18).

The patient was allowed food immediately if the procedure was done under local anesthesia or after 6 hours if under general anesthesia. However, he or she may immediately resume normal activities if neurologically stable.

The specimen was fixed in formalin and sent to Pathology Laboratory. It was processed with isopropyl alcohol and dealcoholized with Xylene. It was then

embedded in paraffin wax and incubated at 50 - 58^{0}C and preserved. With Leica RM2125RTS® Microtome, the specimen was trimmed and sliced to 4 µm thickness and spread over glass slides. It was then stained with hematoxylin and eosin stains and mounted on a microscope and observed. The results were interpreted by a senior Pathologist and reported. It took normally 4 to 7 days for the specimen to be reported. The collected data were analyzed statistically as described below.

STATISTICAL ANALYSIS

The variables were collected from the observed data, and were analyzed by SPSS software version 17.0. Univariate and Multivariate analysis of the variables were done to establish relationships between each other for any association. Pearson's chi square test was applied for the analysis.

A p value of < 0.05 was taken as significant.

A scanogram showing the base containing the fiducials attached to scalp. The 3 fiducials can be seen as radio opaque dots on the base.

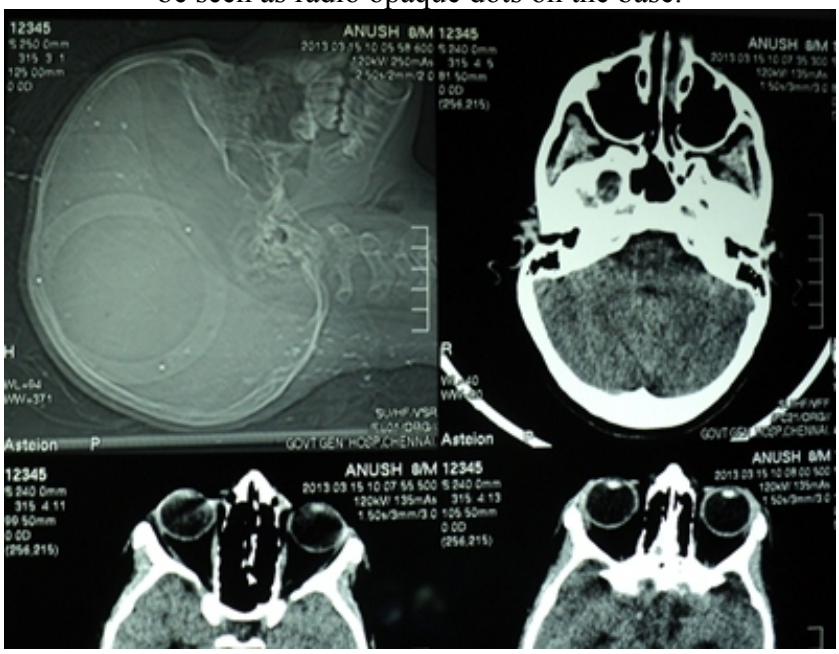

Fig 1: scanogram with the base attached to scalp

Axial non contrast CT image showing a hyperdense lesion in the region of thalamus diplacing III ventricle to left side. (patient no.35). The frame is also noted over scalp.

fig 2:CT showing hyperdense tumor in Right thalamus

MRI T1 WI in coronal section showing the thalamic lesion iso intense to white matter

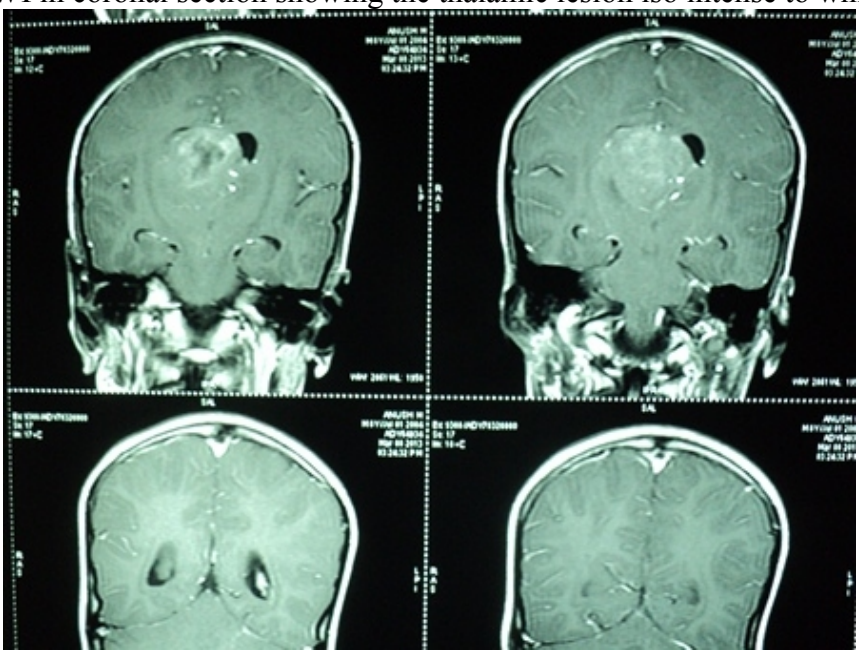

Fig 3: T1 Weighted Image

FLAIR images of the same patient in a sagittal view showing involvement of thalamus and III ventricle

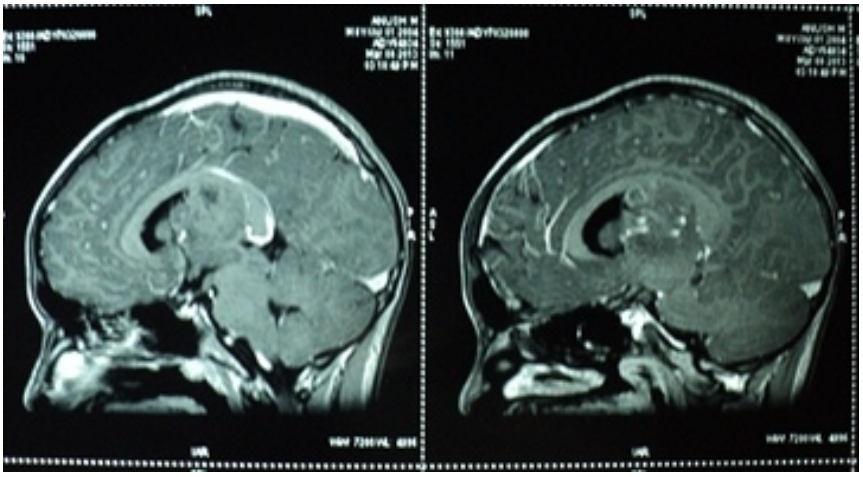

Fig 4: FLAIR image

The phantom base with measuring scales for the three coordinates.

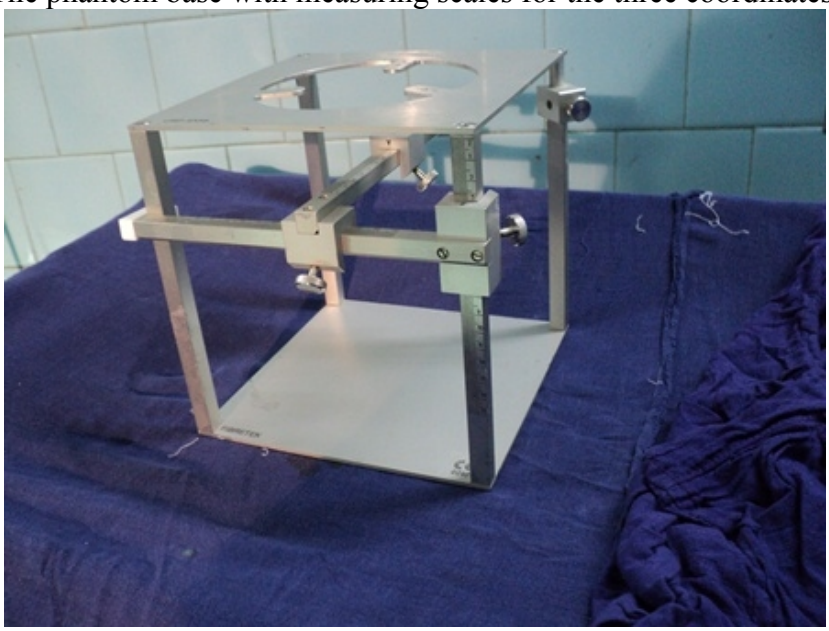

Fig 5: Phantom Base

Phantom base with frame attached on it.

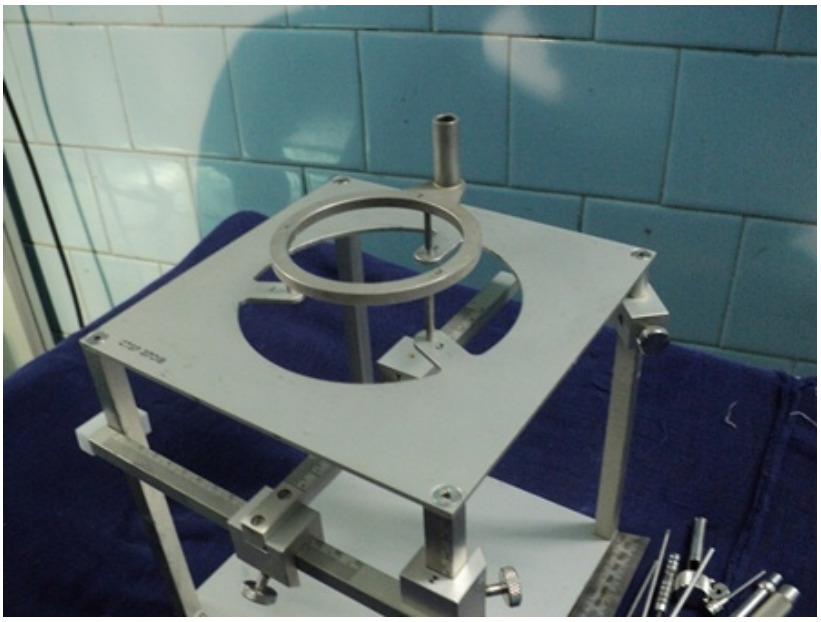

Fig 6: phantom base with holding frame attached

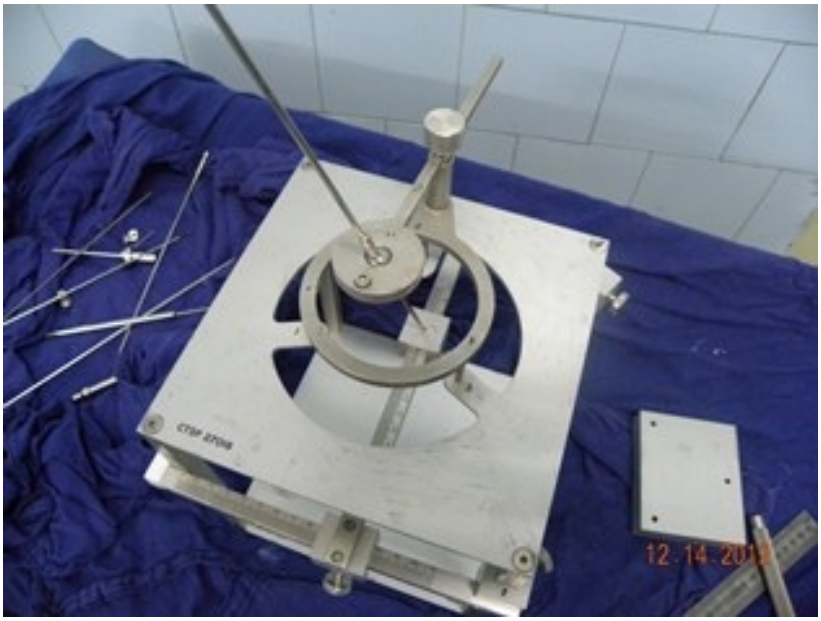

fig 7: Phantom base with frame and calibrated biopsy needle to the location ready for use

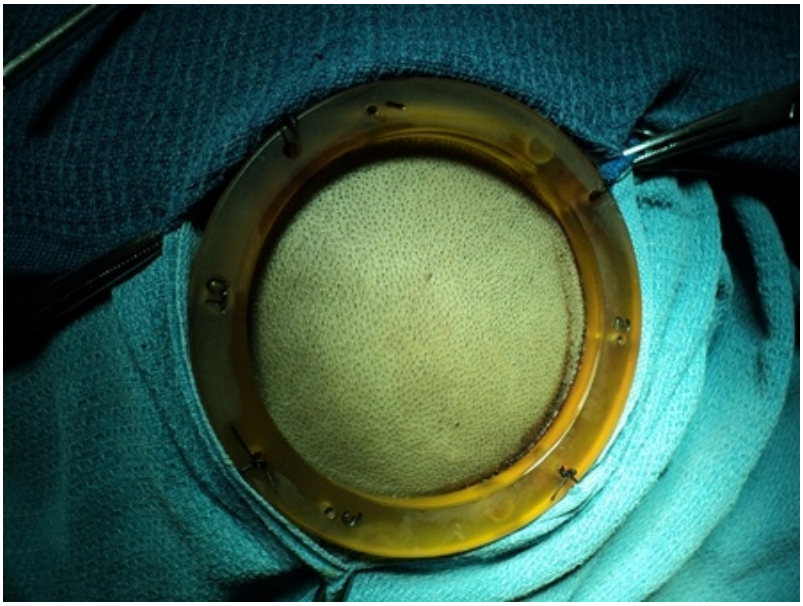

fig 8: CT base with the fiducials attached to scalp. Patient lies on operating table. Operative site was painted and draped.

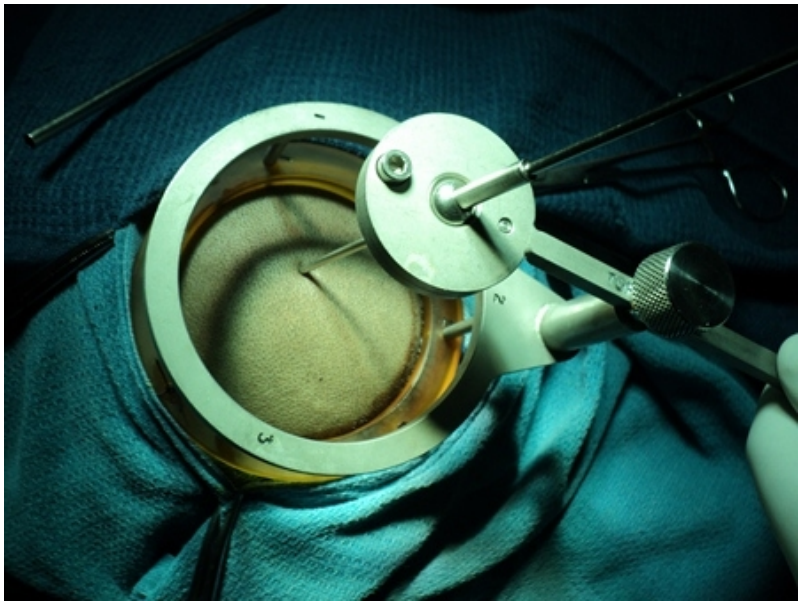

Fig 9: site of burr hole marked.

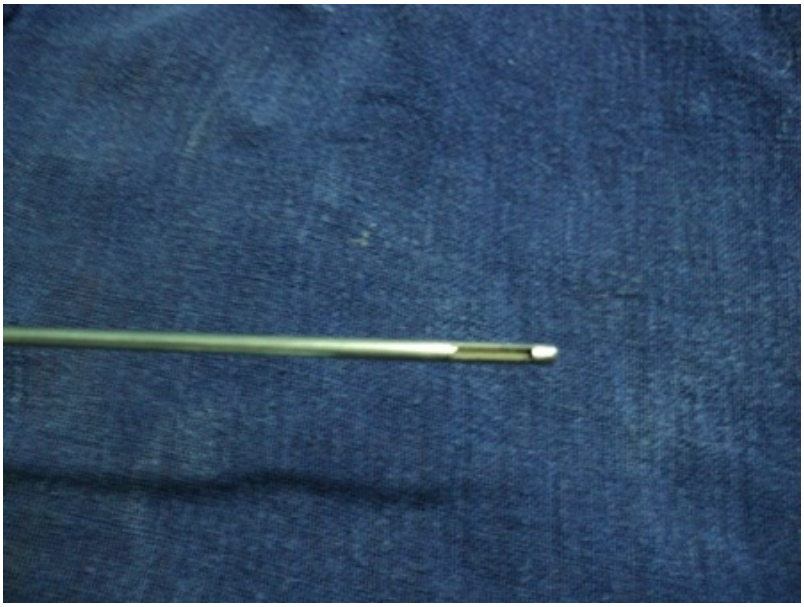

Fig 10: side cutting needle opened

Fig 11: side cutting needle closed

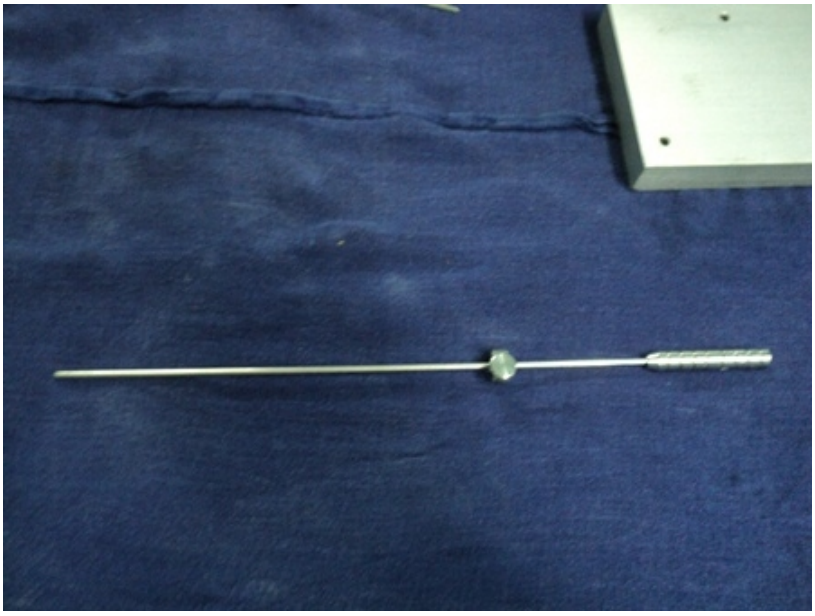

Fig 12: biopsy needle

Fig 13: resected specimen

fig 14: leg 1 of fiducial with Cartesian coordinates marked. He was a recurrent case of anaplastic astrocytoma earlier operated and post irradiation status. The final biopsy report was glioblastoma (patient no.31)

fig 15: leg 2 of fiducial with Cartesian coordinates marked

fig 16:leg 3 of fiducial with Cartesian coordinates marked

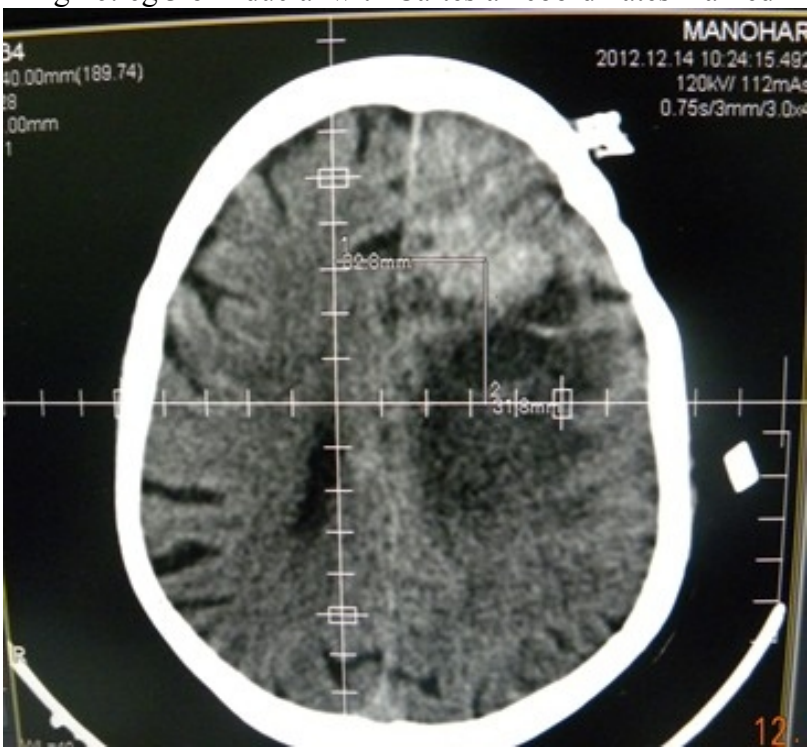

fig 17: tumor site marked

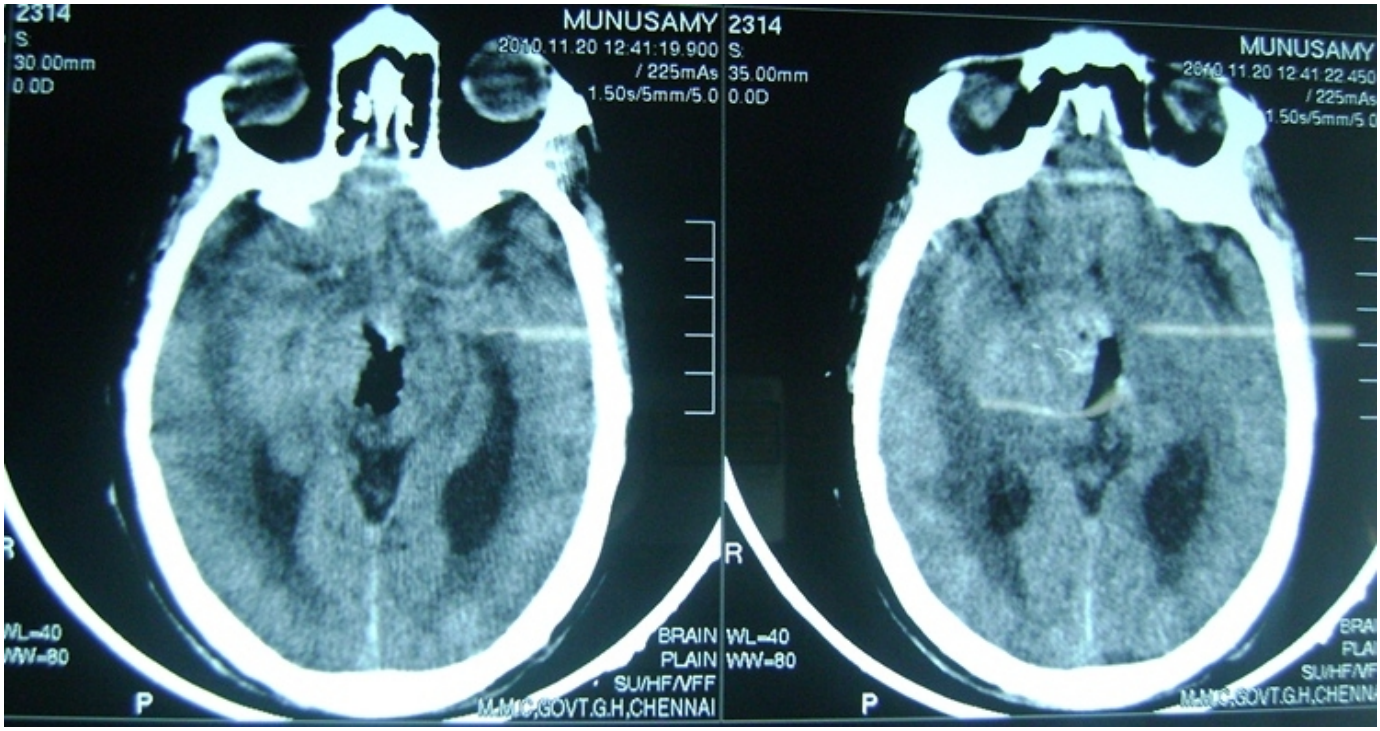

Fig 18: CT image showing post procedural changes. In this image air is present at biopsy site confirming the biopsy at the desired site. There was no hemorrhage in this case (patient no 1).

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OBSERVATIONS AND RESULTS

OBSERVATIONS AND RESULTS

The observations made in the study were analyzed with relevant statistical methods.

1.AGE

Distribution of Age among the Study Population

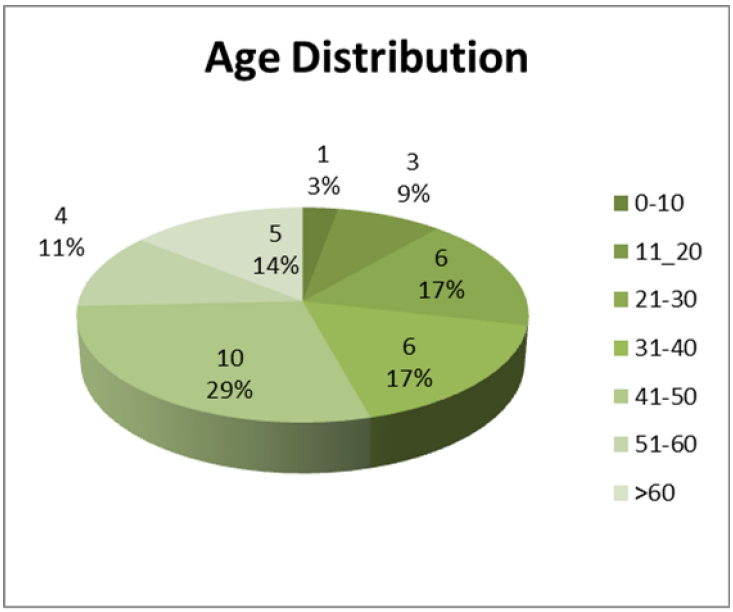


Diagram 1

The age distribution in this study was as noted above. 54% of the patients enrolled in this study were aged above 40 years. The youngest patient was aged 8 years and the eldest, 68 years. The mean age was 39.71 years. There were 4 children included in the study. (ref Diagram 1).

2. GENDER

The distribution of Gender in the series

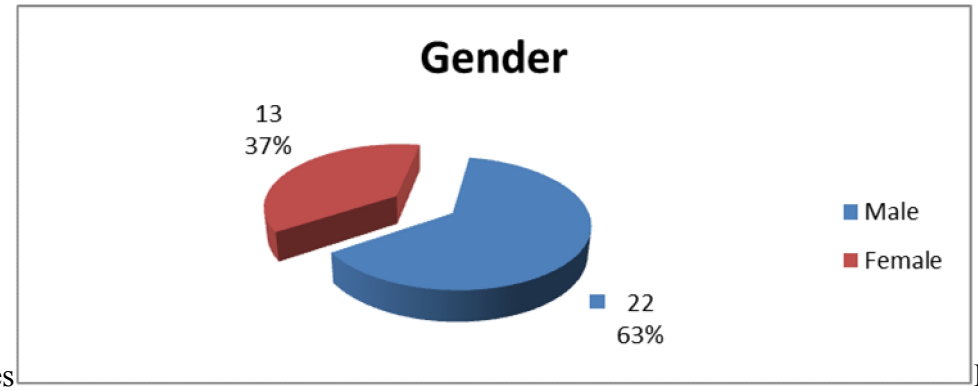


Diagram 2

The gender distribution was as noted in the above pie chart. There were 13 females and 22 males included in the study.

3. PATHOLOGY

Diagnostic Yield

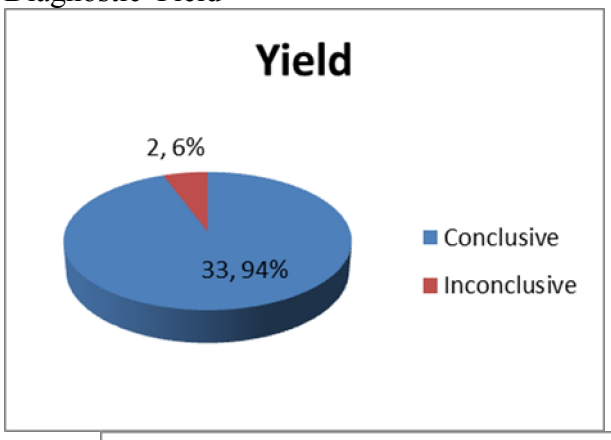


Diagram 3
Grades Of Astrocytoma In This Series

Astrocytoma And Other Lesions

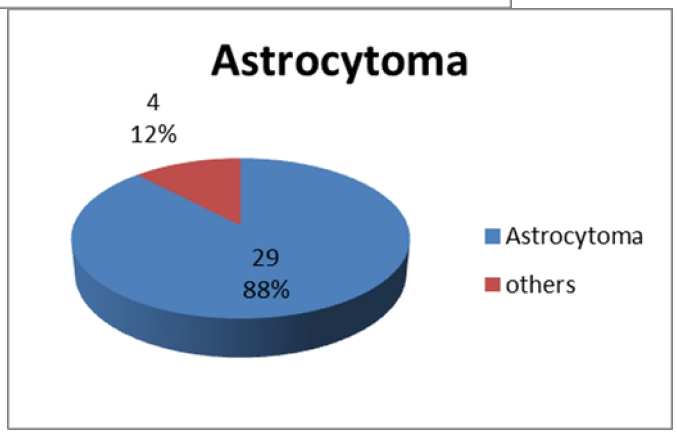


Diagram 4
Other Pathologies

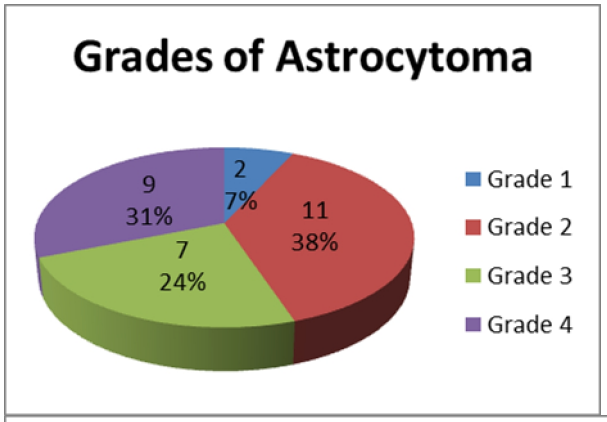


Diagram 5

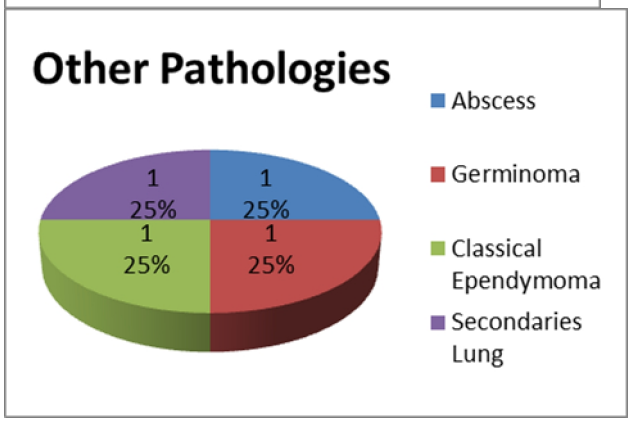


Diagram 6

The diagnostic yield of this study was 94%. (diag. 3). Among 35 cases there were 2 cases reported as inconclusive. The commonest diagnosis reported in this study was astrocytoma. Among those which yielded a conclusive diagnosis, 1 was non neoplastic, 1 was a secondary from lung. 29 cases were astrocytomas. (Diag. 4). The rest were germinoma and classical ependymoma, one each. (Diag. 6)

Among the astrocytomas, 13 were low grade, and 16 were high grade astrocytomas.(Diag.5). *Chandrasoma PT et al*[12] investigated the accuracy of image-guided STB in 30 cases, and found that it was accurate in 28 of the 30 cases. They concluded that with careful placement of needle, STB can accurately reach the target and yield sufficient for management.

3. SITE OF LESION

Distribution of location of the lesion in the study

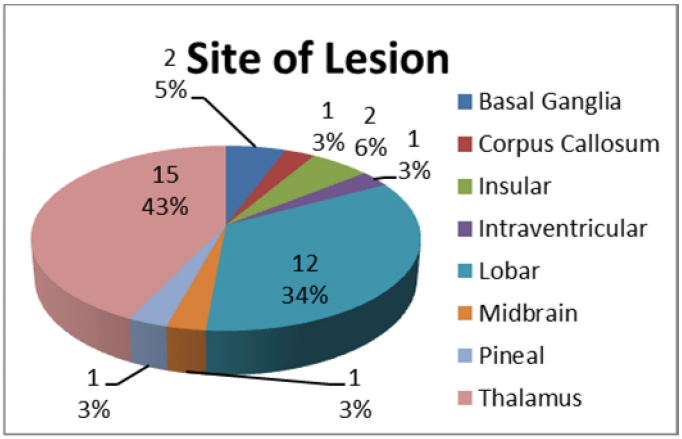


Diagram 7

Lobar Lesions

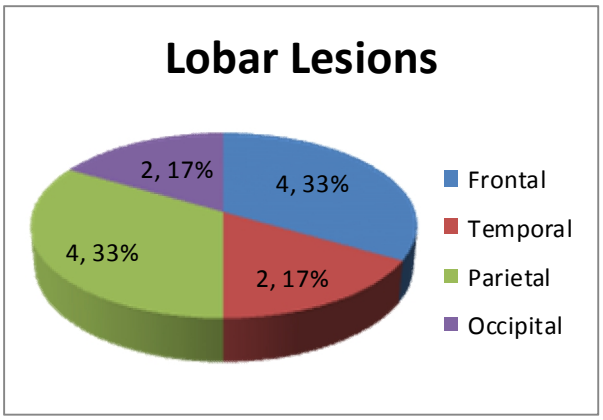


Diagram 8

The commonest sites of lesions in the study were the region of thalamus and lobar region (43% & 34% respectively) (Diag.7). Other sites included deeper regions like midbrain, corpus callosum, basal ganglia, pineal and intraventricular region. Among the lobar lesions the distribution was more or less equal, frontal 4, temporal 2, parietal 5, and occipital 2(Diag.8). There were 12 (33%) superficial lesions, and others were deep seated ones.

Distribution of Side in the study

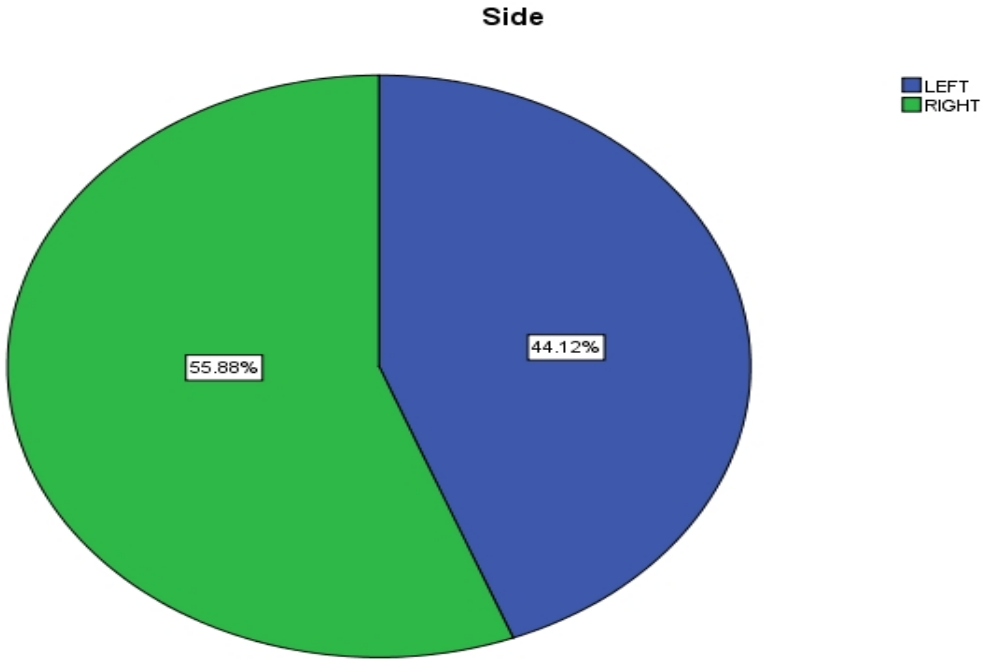


Diagram 9

Right sided lesions were more in number (55.88%). But this was not significant statistically. There were 20 Right sided lesions and 15 Left sided lesions. (Diag.9).

4. GENERAL ANESTHESIA

Type of anesthesia

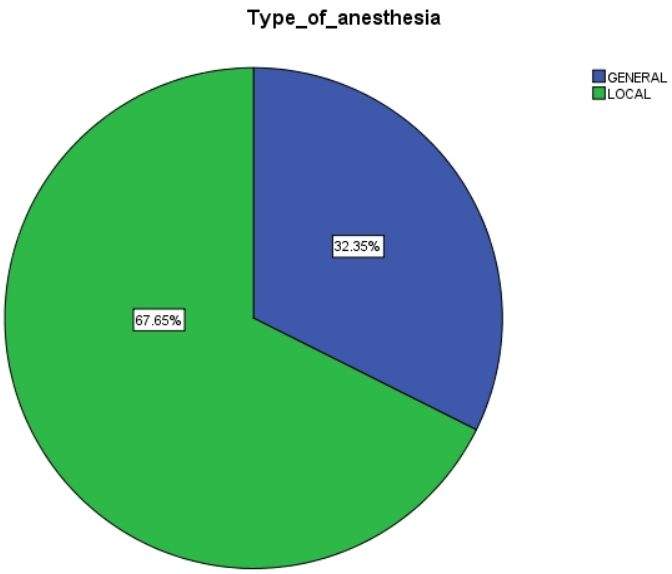


Diagram 10

Majority of the lesions were operated under local anesthesia (67.65%)(Diag.10). The choice of anesthesia was decided by the anesthesiologist. Children, patients with poor neurological status, and poor Karnofsky Score were operated under general anesthesia. There was no conversion of local anesthesia to general anesthesia. All patients recovered from general anesthesia within 15 – 25 minutes.

5. COMPLICATION

Complication Rate observed in the study

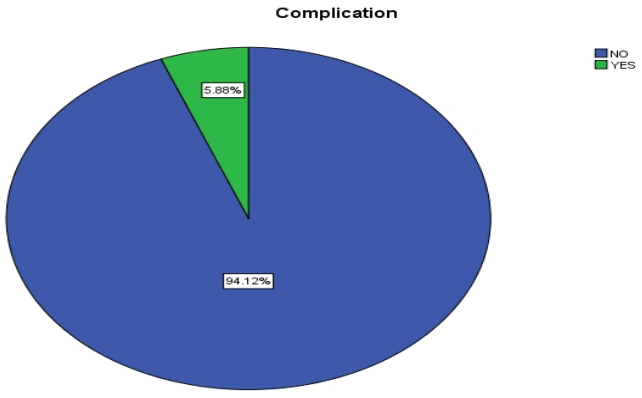


Diagram 11

There were two post-operative events of hemorrhage. Both were managed conservatively. One patient had transient deterioration in cognition level, which

recovered well on conservative management. The other patient clinically remained stable neurologically and had an uneventful course (Diag. 11).

There was one death in the post-operative period, 30 days after the procedure. She was diagnosed with anaplastic astrocytoma and was transferred to Radiotherapy Department in a stable condition. There she deteriorated progressively and died. It may be safely concluded that the death was unrelated to the procedure but to the progression of the disease process itself. There was no case of infection, even in the one case operated for gangliocapsular abscess.

6. POST OPERATIVE MANAGEMENT

Post-operative Management

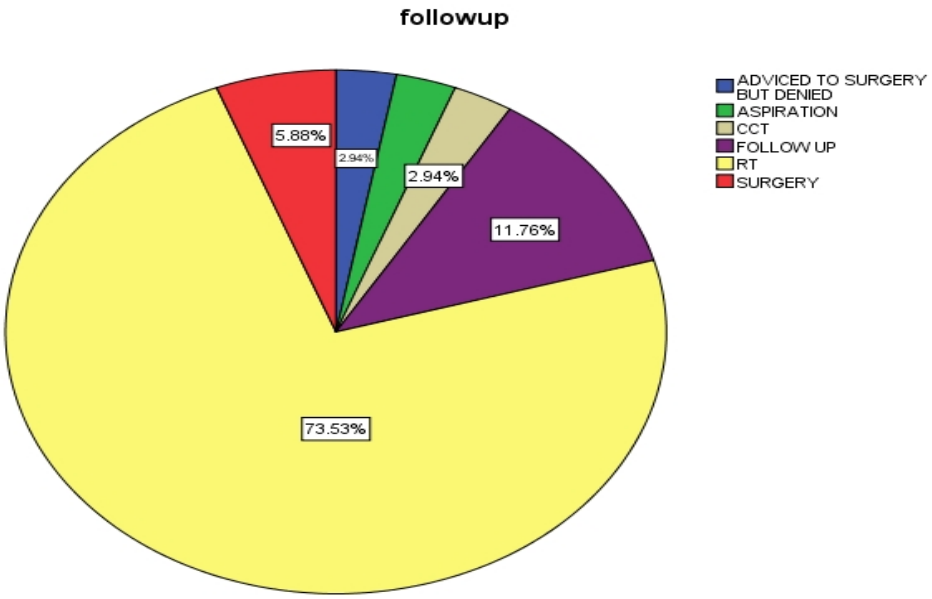


Diagram 12

The postoperative management of the patients undergoing stereotactic biopsy was detailed in the previous pie chart (Diag.12). Majority (73.53%) of the patients was referred for radiotherapy, few (11.76%) were on close follow up

with serial radiological investigations, and four patients were advised surgical resection, among whom one refused. The patient with metastasis from lung was referred to Department of Medical Oncology for further management. The one non-neoplastic case – a deep seated abscess required no more aspiration as it resolved on further CT follow up.

COMPARISON OF VARIOUS FACTORS AMONG EACH OTHER FOR ASSOCIATION

Further analysis of the observed findings with statistical analysis was as follows:

1. **Age and gender**

Comparing age groups along gender

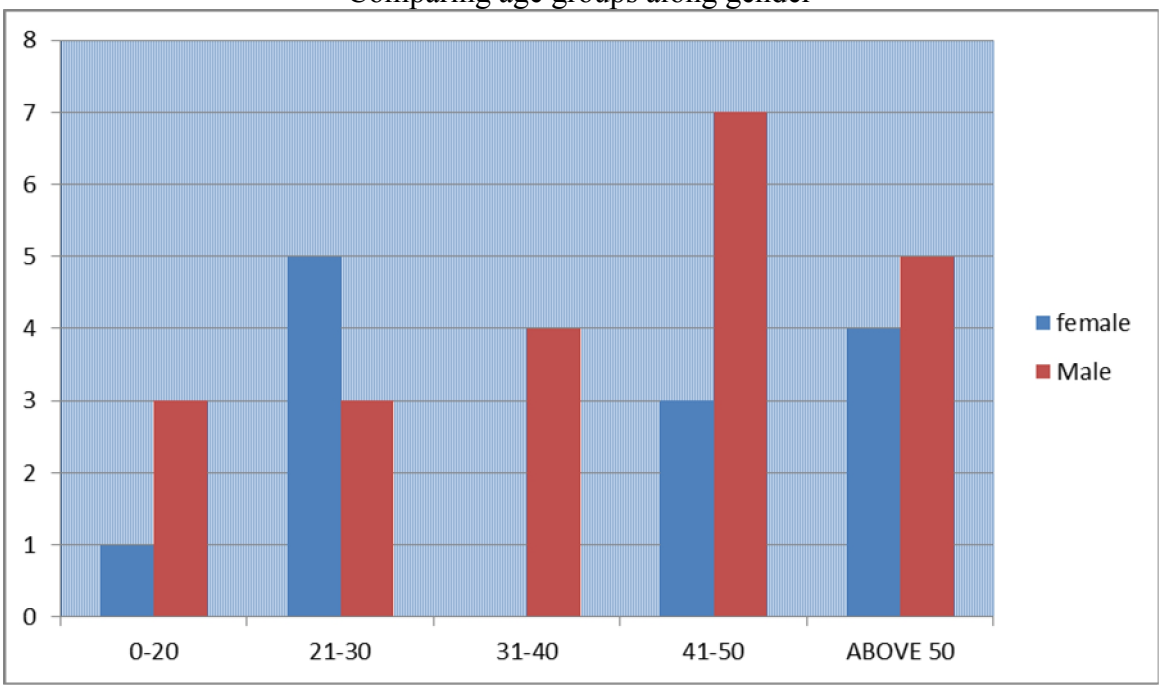


Diagram 13

Table of age groups and gender

Age	F	M	Total
0-20	1	3	4
21-30	5	3	8
31-40	0	4	4
41-50	3	7	10
ABOVE 50	4	5	9
Total	13	22	35

Table 1

The relationship between age and gender is shown in Diagram 13 and Table 1. Age groups were evenly distributed between both genders. In the age group of 31 – 40 there was no female patient. There was no statistical significance in the plot.

2. Age and diagnosis

Relationship of age and diagnosis

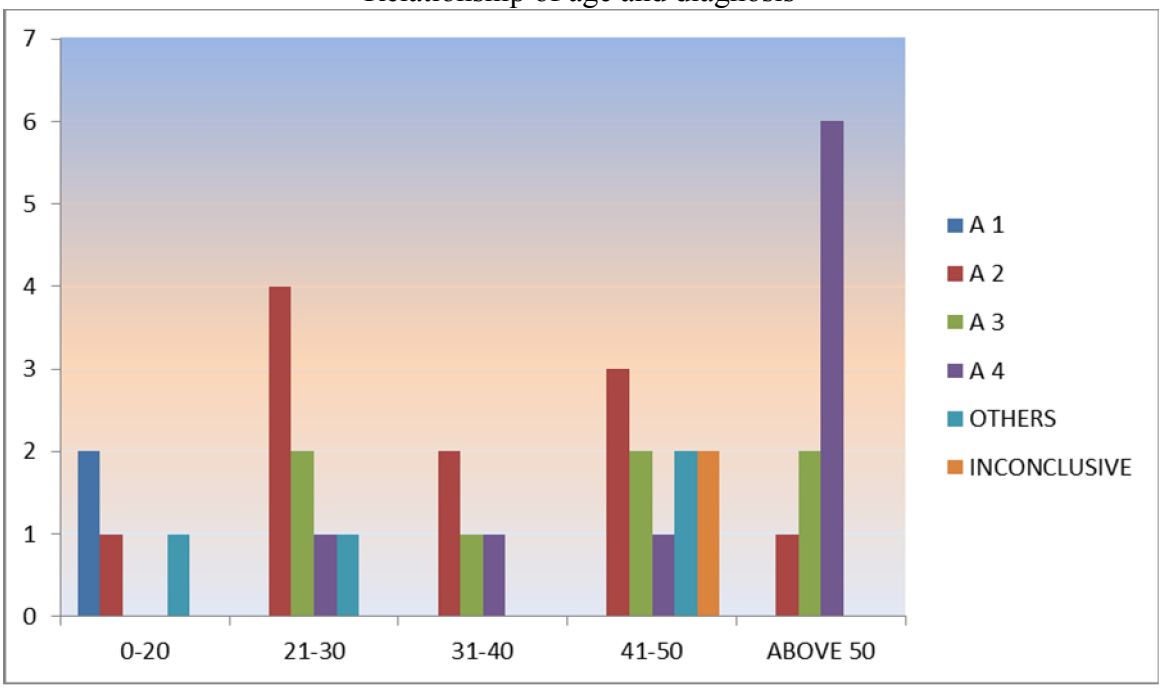


Diagram 14 (A1 – Astrocytoma Gr I, A2 – Astrocytoma Gr II, A3 – Astrocytoma Gr III, A4 – Astrocytoma Gr IV)

Table of age and diagnosis

Age	A 1	A 2	A 3	A 4	OTHERS	INCONCLUSIVE	TOTAL
0-20	2	1	0	0	1	0	4
21-30	0	4	2	1	1	0	8
31-40	0	2	1	1	0	0	4
41-50	0	3	2	1	2	2	10
ABOVE 50	0	1	2	6	0	0	9
Total	2	11	7	9	4	2	35

Table 2

Table 3: **Statistical Analysis of Age and Pathology**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	35.214	20	.019
Likelihood Ratio	30.230	20	.066
N of Valid Cases	35		

The comparison of age with diagnosis showed that grade I astrocytomas are exclusively present in children [2/2]. There was an increasing trend towards higher grades of astrocytoma with increasing age. Grade IV astrocytomas are seen more in the age group of >50 years. These findings were statistically significant. (Diagram 14, Table 2 & 3). The diagnosis of germinoma and ependymoma were also associated with children. So the observation of age influencing the diagnosis was significant (p = 0.019).

Tsermoulas G et al[36] analyzed the association of various factors influencing the yield of needle biopsy of brain, and concluded that young age influenced the yield negatively, and tumor volume had a positive influence on yield.

3. Age and location

Comparing age with location of lesions, it was noticed that pineal and intraventricular locations were exclusively seen among patients of younger age, and other lobar and deep seated locations were equally distributed among adult patients across various age groups(Diagram 15, Table 5). These findings were not significant.

Zacharia BE et al[37] compared open resection and stereotactic biopsy for pineal tumors and found that STB had a mean diagnostic yield of 94%, with morbidity of 1.3% and mortality of 8.1%.

Comparison of age groups and locations of lesion

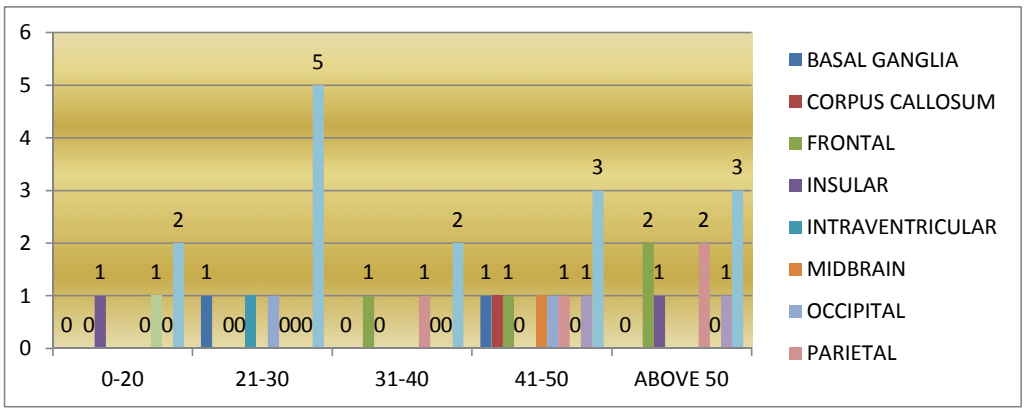


Diagram 15: showing age and location

Age and location

Age group	BASAL GANGLIA	CORPUS CALLOSUM	FRONTAL	INSULAR	INTRAVENTRICULAR	MIDBRAIN	OCCIPITAL	PARIETAL	PINEAL	TEMPORAL	THALAMUS	Total
0-20	0	0	0	1	0	0	0	0	1	0	2	4
21-30	1	0	0	0	1	0	1	0	0	0	5	8
31-40	0	0	1	0	0	0	0	1	0	0	2	4
41-50	1	1	1	0	0	1	1	1	0	1	3	10
ABOVE 50	0	0	2	1	0	0	0	2	0	1	3	9
Total	2	1	4	2	1	1	2	4	1	2	15	35

Table 5: age and location

4. Age and anesthesia

Age and anesthesia depicted for analysis

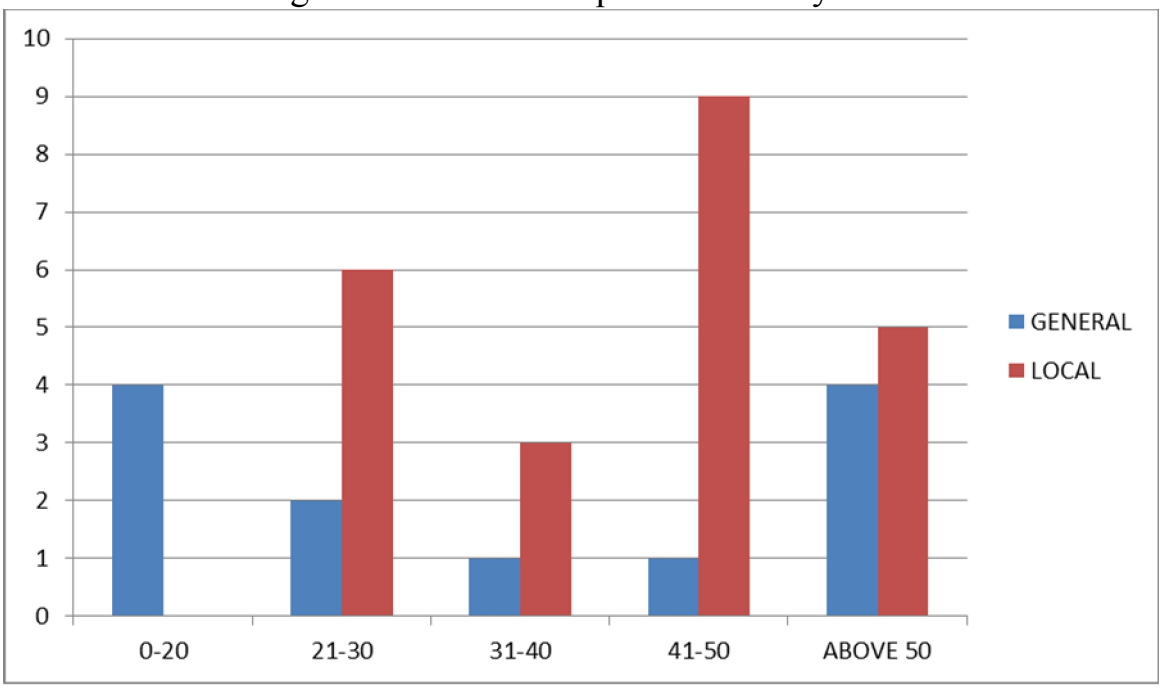


Diagram 16: Showing age and anesthesia

Age plotted against anesthesia

Age	GENERAL	LOCAL	Total
0-20	4	0	4
21-30	2	6	8
31-40	1	3	4
41-50	1	9	10
ABOVE 50	4	5	9
Total	12	23	35

Table 6

Table 7 : statistical analysis showing significance

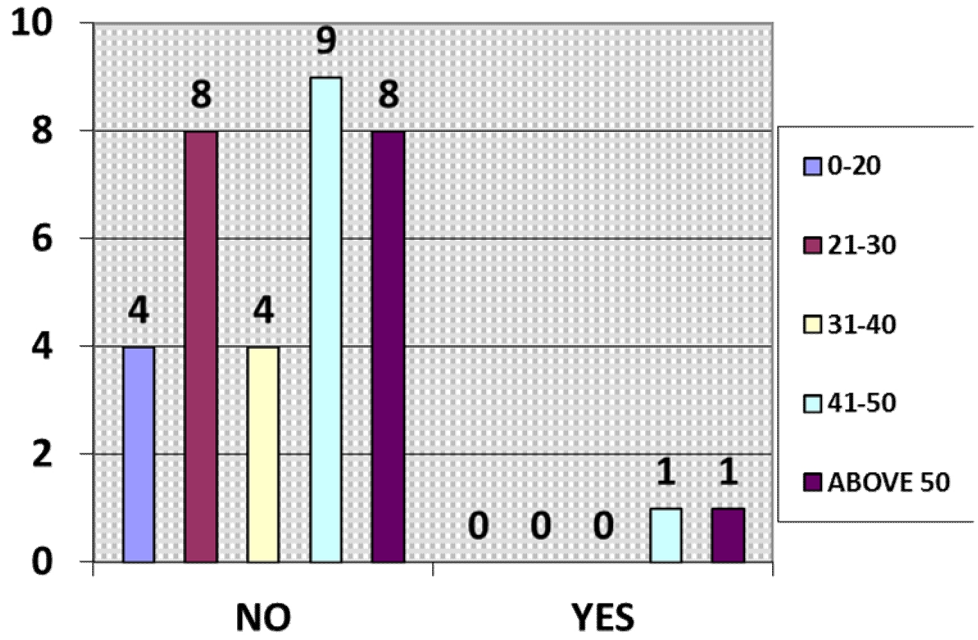
statistical analysis	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	11.156[a]	4	.025
Likelihood Ratio	12.641	4	.013
N of Valid Cases	35		

a. 7 cells (70.0%) have expected count less than 5. The minimum expected count is 1.37.

The choice of anesthesia showed an increased administration of general anesthesia (GA) in extremes of age. It showed a bi-modal trend in which younger and elder patients were given GA. Age was a factor in influencing the administration of GA (Diagram 16, Table 6). This finding was statistically significant (P = 0.025) (table 7).

5. Age and complication

Diagram17: Showing age and complication



Age and complication

AGE	NO	YES	Total
0-20	4	0	4
21-30	8	0	8
31-40	4	0	4
41-50	9	1	10
ABOVE 50	8	1	9
Total	33	2	35

Table 8

In this study, 2 patients had complications of haemorrhage which were noticed in post operative CT scan. Both were managed conservatively. They both were persons aged more than 40 years (Diagram 17,Table 8). But this finding was

not statistically significant to establish the association of increasing age with complication.

In their study, *Parreno MG et al*[38] performed frameless stereotactic procedure on 18 pediatric patients. The diagnostic yield was 100%, and the operative mortality was nil. They encountered two hemorrhagic complications, and one transient deficit. They have concluded that stereotaxy was accurate, and safe on children.

Meshkini A et al[39], in their study on 172 children over a period of 17 years, found that brain stem was the most common location, and glioma was the most common diagnosis. Others were metastatic, lymphoma,oligodendroglioma, craniopharyngioma, pineocytoma, and other non neoplastic lesions.

(6) Age and condition at discharge

	Condition.at.Discharge				
AGE	D T	E	I	S	Total
0-20	0	0	3	1	4
21-30	0	1	1	6	8
31-40	0	0	1	3	4
41-50	0	0	4	6	10
ABOVE 50	1	0	1	7	9
Total	1	1	10	23	35

Table 9 : Age and condition at discharge plotted against each other

There was one death in the age group between 20-30 years (Table 9). There was one patient in the age group 41-50 years which had a transient deterioration in neurological status.

(7) Gender and diagnosis

Diagram 18 : diagram depicting distribution of diagnoses across age

	DIAGNOSIS				
SEX	A	A 2	A 3	A 4	INCONCLUSIVE
F	0	7	2	2	1
M	2	4	5	7	1
Total	2	11	7	9	2
	5.7%	31.4%	20.0%	25.7%	5.7%

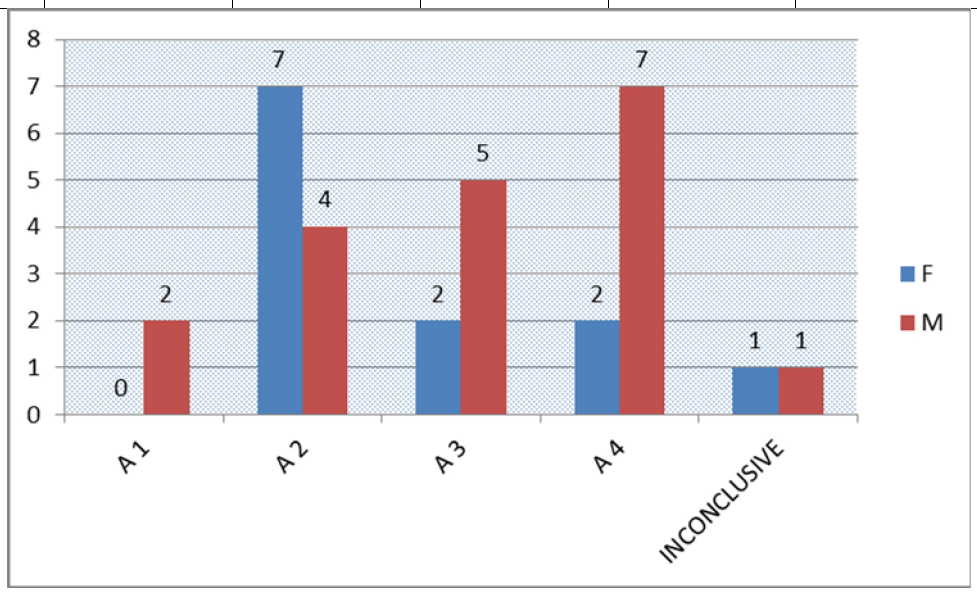


Table 10 : gender plotted against diagnosis

Female patients had a tendency to have low grade glioma than males one increasing diagnosis was in each gender.this was not statistically significant(Diagram 18,Table10). It can be safely concluded that gender has not been found to have any role in influencing diagnosis. One of ependymoma was

observed in male gender. Male children were more prone to develop ependymoma than female children.

(8) Gender and location

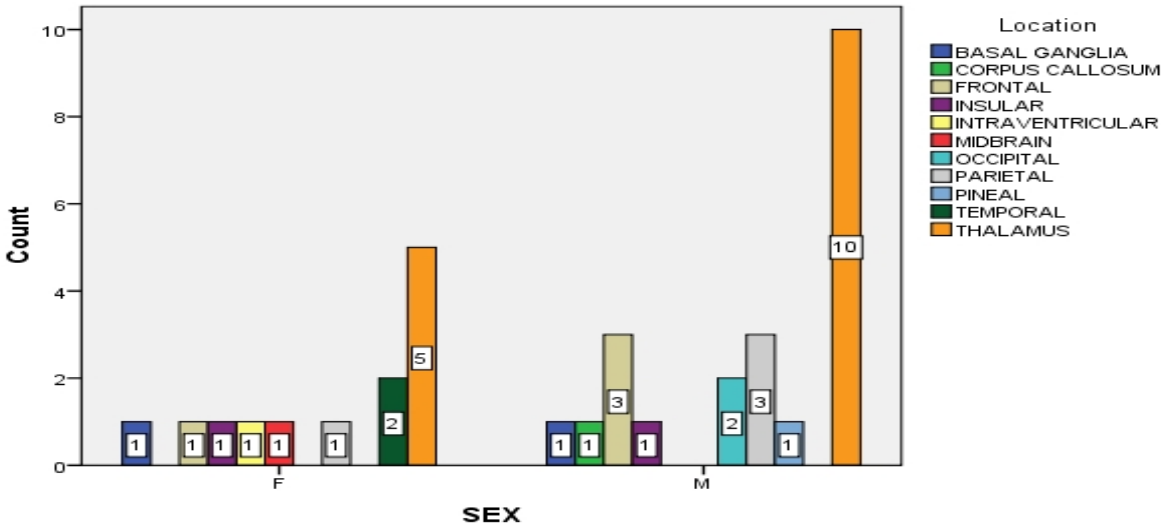


Diagram 19 : Gender and Location of the Pathology

Pineal region corpus collasal region were observed to have lesions in male gender. Males were observed to devolope thalamic lesions than females(Diagram 19). But this was not statistically significant.

(9) Gender and complication

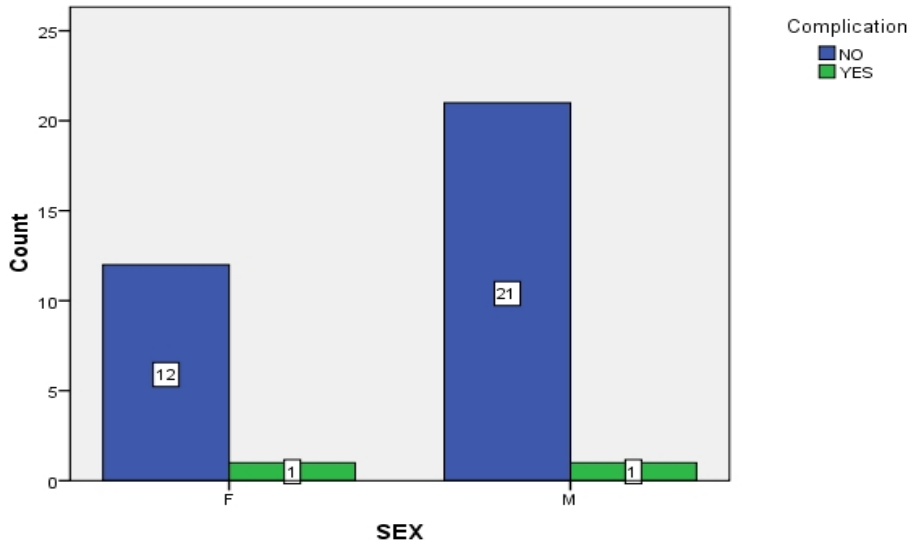


Diagram 20 :Gender and Complications

	Complication		
SEX	NO	YES	Total
F	12	1	13
M	21	1	22
Total	33	2	35
	94.3%	5.7%	100.0%

Table 11 : Table showing Gender Plotted on complications

One hemorrhagic complication was noted in each gender(Diagram 20,Table11).

There was no finding of infection.

(10) Gender and condition at discharge

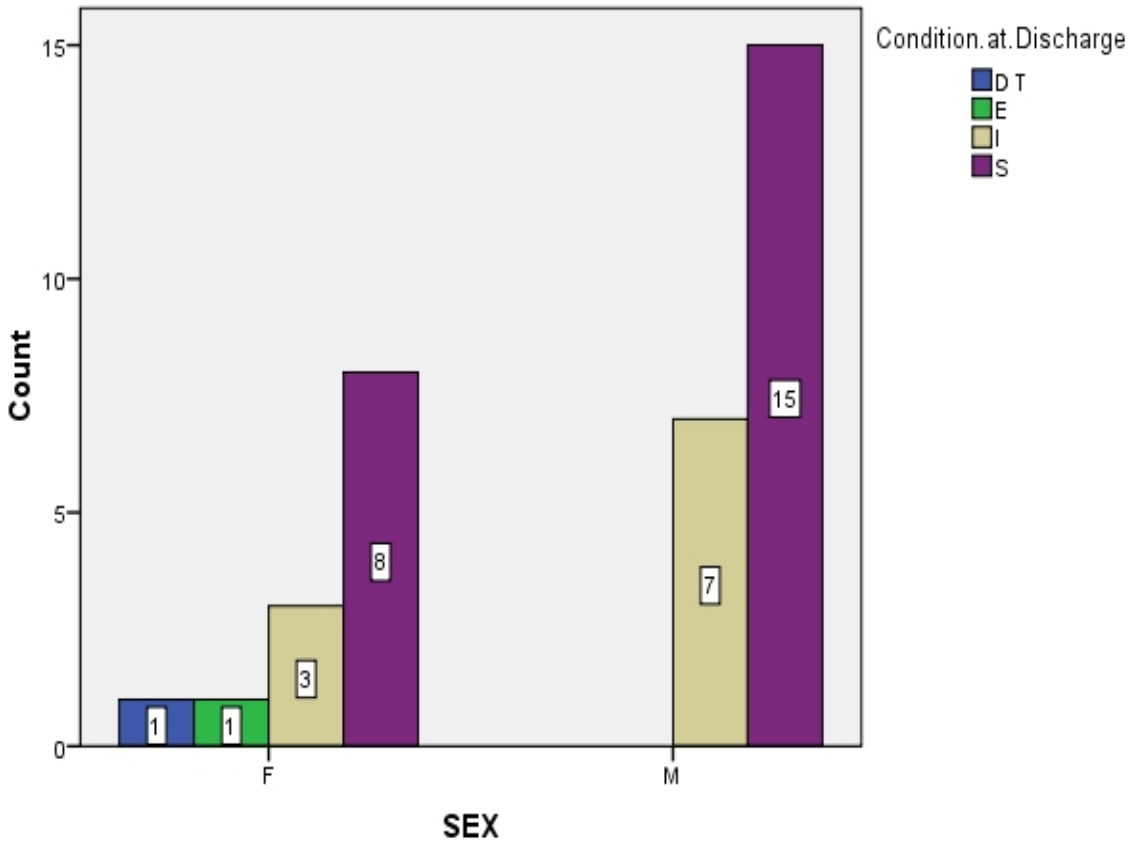


Diagram 21 : Diagram depicting Gender and Condition at Discharge

Condition.at.Discharge					
SEX	D T	E	I	S	Total
F	1	1	3	8	13
M	0	0	7	15	22
Total	1	1	10	23	35
	2.9%	2.9%	28.6%	65.7%	100.0%

Table 12 : Gender And Condition At Discharge

One patient who had transient deterioration of neurological status and another who died were both females(Diagram 21,Table12). But this finding was also not statistically significant.

(11) Deep seated lesions and diagnosis

Comparing deep seated lesions and diagnosis for any association influencing the diagnosis, it was observed that both negative diagnosis were present in deep seated lesions(Diagram 22,Table13). But this had no statistical significance.

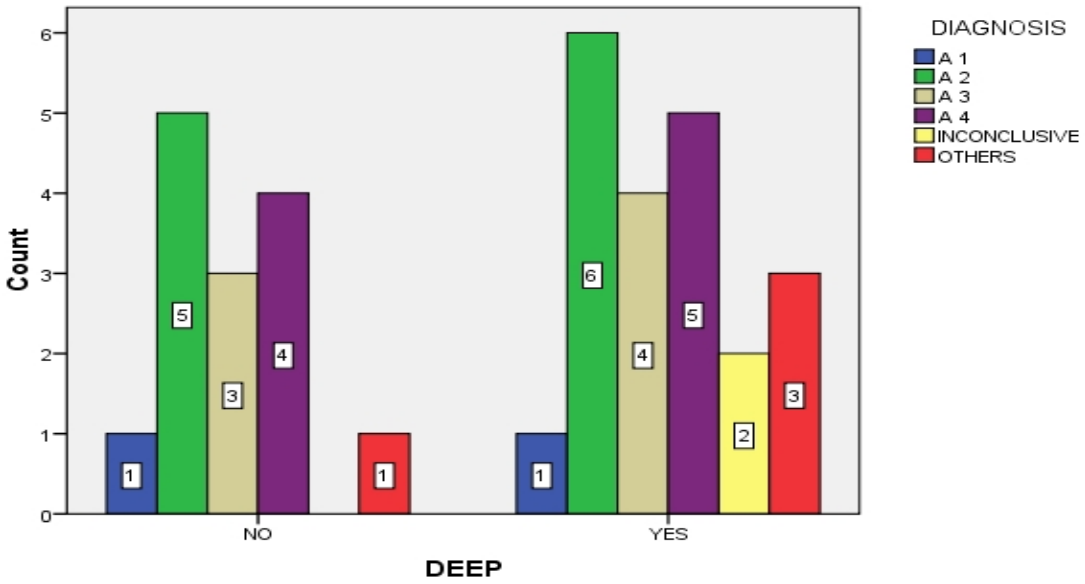


Diagram 22 : deep seated lesions and diagnosis

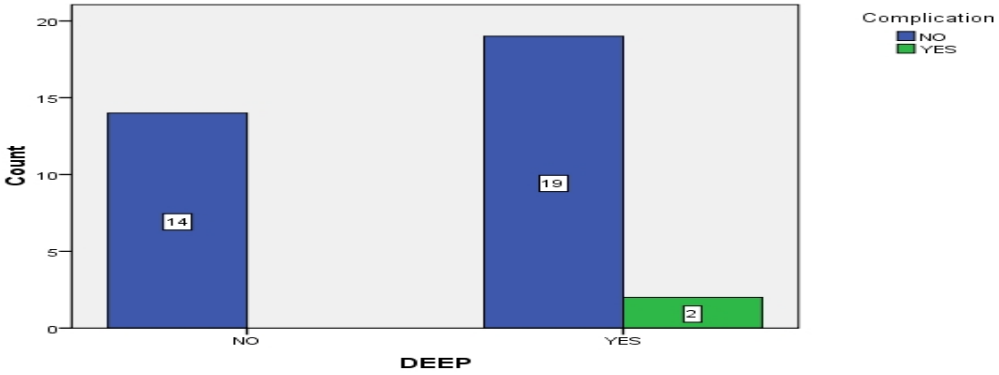
DIAGNOSIS					
DEEP	A 1	A 2	A 3	A 4	INCONCLUSIVE
NO	1	5	3	4	0
YES	1	6	4	5	2
Total	2	11	7	9	2
	5.7%	31.4%	20.0%	25.7%	5.7%

Table 13 : Deep seated lesions and diagnosis

(12) Deep-seated lesions and complications

Both the patients who had complications had deep seated lesions(Diagram 23,Table14) but on statistical analysis it was not found to be significant.

Diagram 23 : Deep Seated Lesions and Complications



Complication			
DEEP	NO	YES	Total
NO	14	0	14
YES	19	2	21
Total	33	2	35
	94.3%	5.7%	100.0%

Table 14 : Table of plot of Deep seated Lesions and Complications

Woodworth GF et al,[40] compared frame based and frameless methods of STB, and observed that frameless STB yielded a biopsy rate of 89%, and morbidity of

6% and mortality of 1%. Deep-seated lesions were 2.7 times less likely to yield the diagnosis than cortical lesions. Cortical lesions required more than one trajectory to yield a positive sample, but this was not associated with increased morbidity.

(13) Deep-seated lesions and condition at discharge

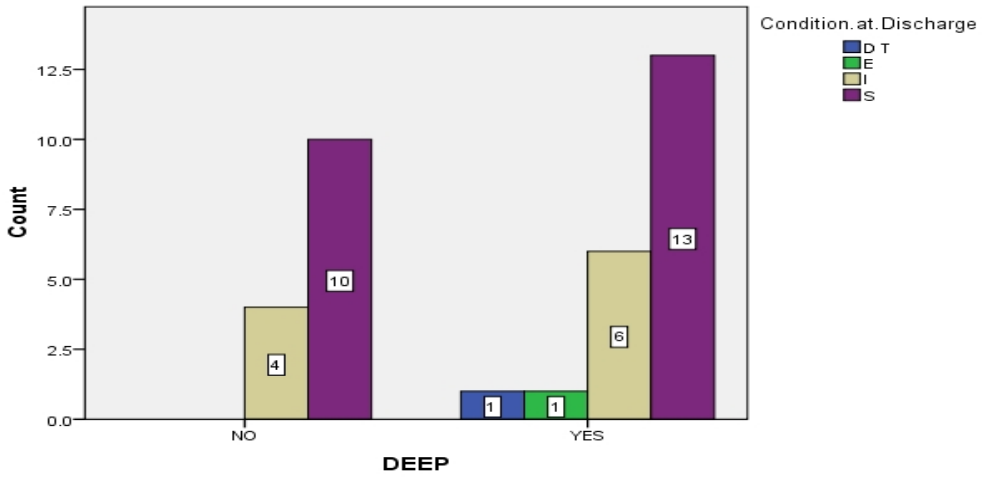


Diagram 24 : Deep seated Lesions and Condition at Discharge

	Condition.at.Discharge				
DEEP SEATED	D T	E	I	S	Total
NO	0	0	4	10	14
YES	1	1	6	13	21
Total	1	1	10	23	35
	2.9%	2.9%	28.6%	65.7%	100.0%

Table 15 : Deep seated lesions and condition at discharge

The patients who had transient neurological deterioration and another patient who had expired both harboured deep seated lesions(Diagram 24,Table15). This

finding was not statistically significant to conclude that deep seated lesions adversely affected the condition at dischage.

(14) Astrocytoma and location

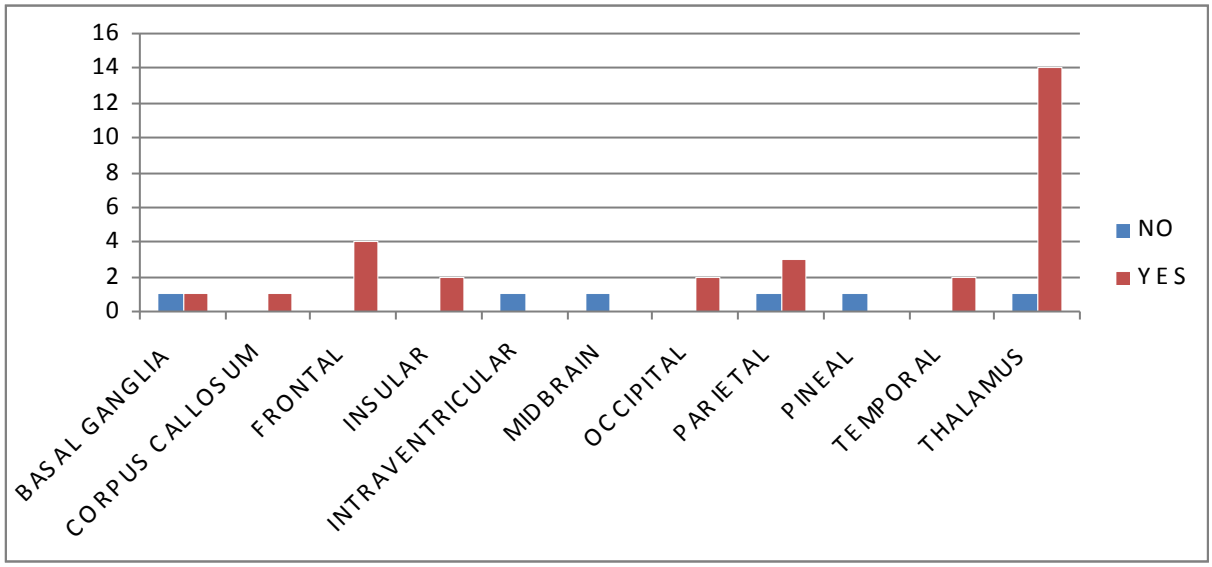


Diagram 25 : Astrocytomas and location of the lesion

	Location											
Astrocytoma	BASAL GANGLIA	CORPUS CALLOSUM	FRONTAL	INSULAR	INTRAVENTRICULAR	MIDBRAIN	OCCIPITAL	PARIETAL	PINEAL	TEMPORAL	THALAMUS	Total
NO	1	0	0	0	1	1	0	1	1	0	1	6
YES	1	1	4	2	0	0	2	3	0	2	14	29
Total	2	1	4	2	1	1	2	4	1	2	15	35
	5.7%	2.9%	11.4%	5.7%	2.9%	2.9%	5.7%	11.4%	2.9%	5.7%	42.9%	100.0%

Table 16 : astrocytoma and location

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	19.629[a]	10	.033
Likelihood Ratio	17.451	10	.065
N of Valid Cases	35		

Table 17 : probability table showing significance of association between astrocytomas and site

Astrocytomas were commonly noticed to be located in thalamus and lobar regions(Diagram 25,Table16). [14/15 cases of thalamus were astrocytomas and 11/12 lobar lesions were astrocytomas]. This finding was statistically significant (p = 0.033) (Table17)

(15) Astrocytoma and complication

	NO	YES	Total
NO	6	0	6
	100.0%	.0%	100.0%
YES	27	2	29
	93.1%	6.9%	100.0%
Total	33	2	35
	94.3%	5.7%	100.0%

Table 18 : Astrocytomas and complications

Both the patients with complications had a diagnosis of astrocytoma(Table18). But this finding was not statistically significant.

(16) Astrocytoma and condition at discharge

	Condition.at.Discharge				
	D T	E	I	S	Total
NO	0	0	4	2	6
YES	1	1	6	21	29
Total	1	1	10	23	35

Table 19 : Astrocytomas and condition at discharge

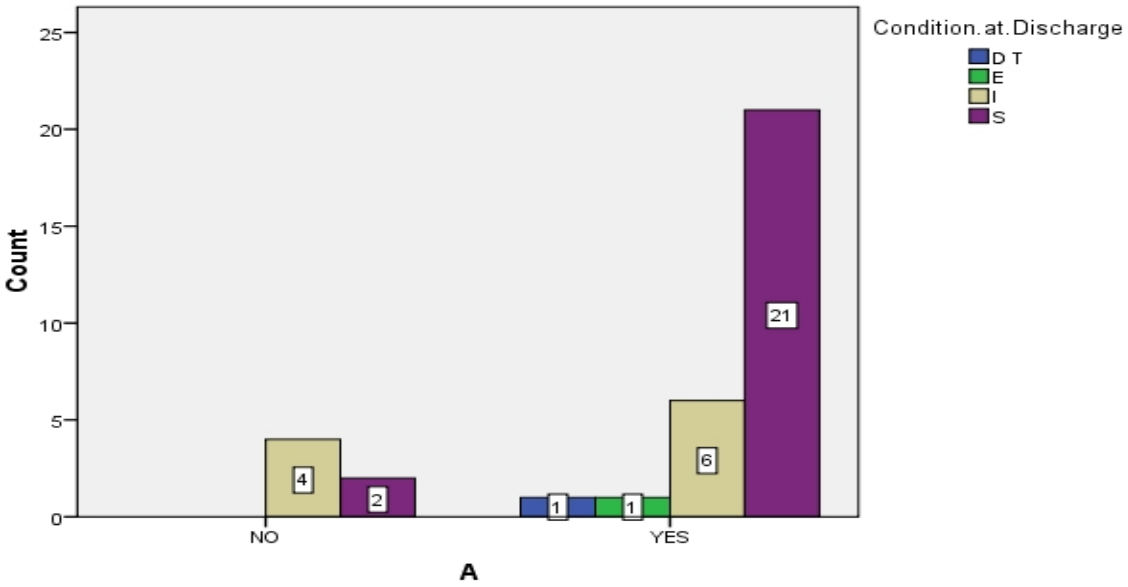


Diagram 26: Astrocytomas and condition at discharge

One patient who had transient neurological deterioration and another patient who died harboured astrocytomas(Diagram 26,Table19). But this was not statistically significant enough to associate the diagnosis of astrocytoma with adverse post operative events.

(17) High grade Astrocytoma and location

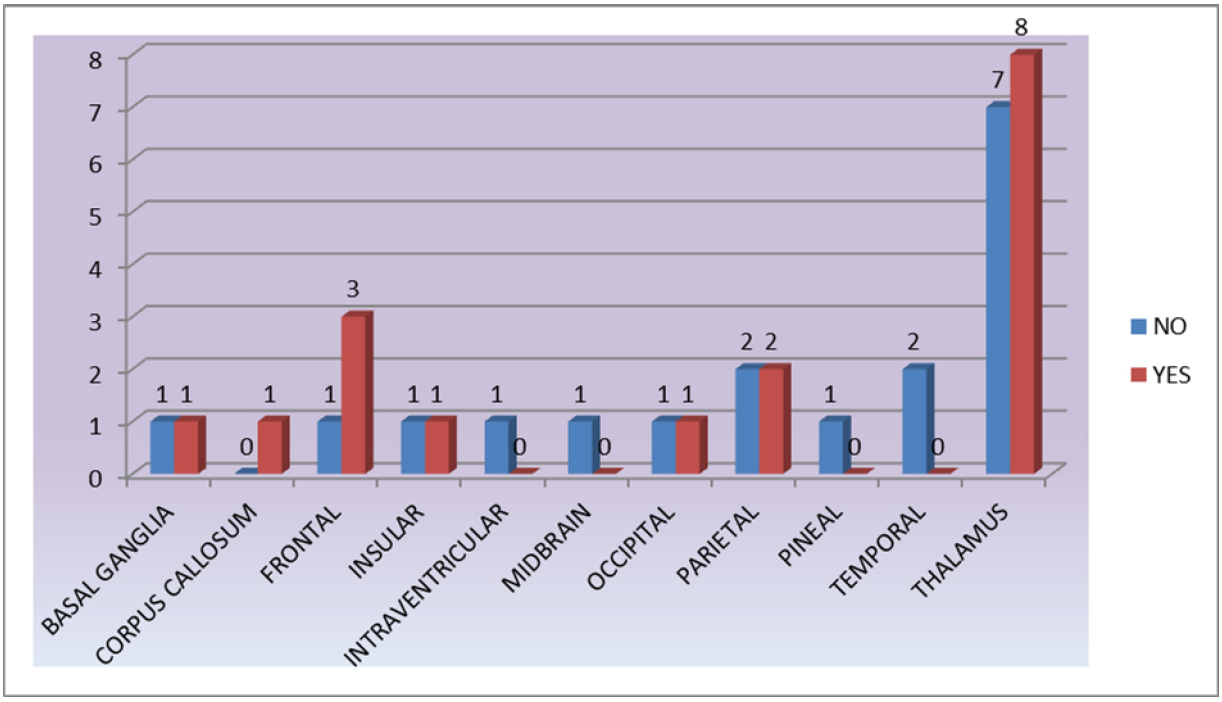


Diagram 27 : High grade astrocytoma and Location

High grade gliomas were present 8 of the 15 cases of thalamus, and 6 out f 12 lobar lesions(Diagram 27). Both high and low grade gliomas were observed to be distributed among all locations.

(18) High grade Astrocytoma and complication

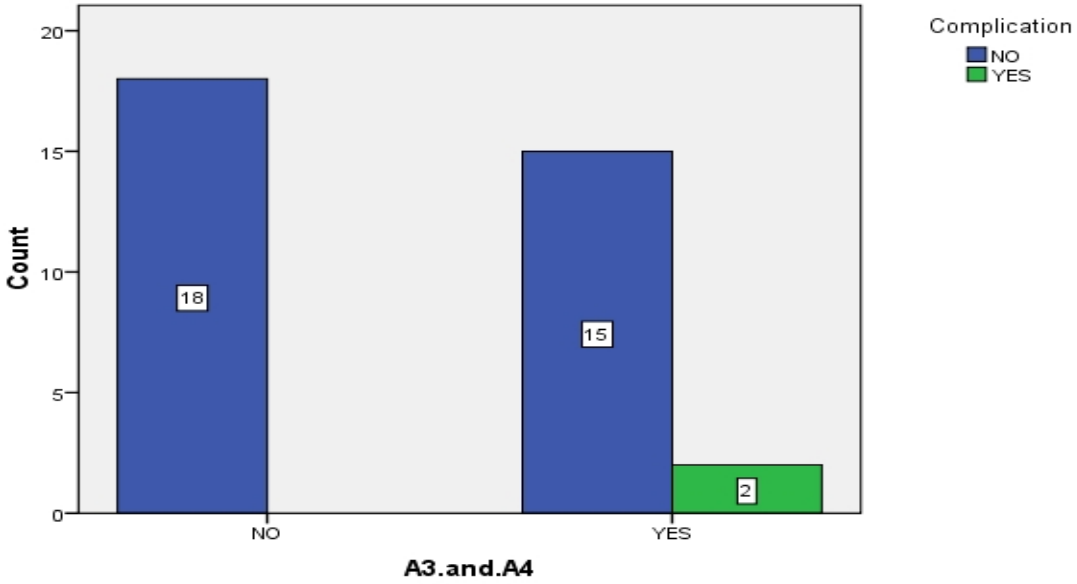


Diagram 28: Comparing high grade astrocytoma and complications

Complication			
A3.and.A4	NO	YES	Total
NO	18	0	18
YES	15	2	17
Total	33	2	35

Table 20 : high grade astrocytomas and complications

Both patients who had complications had high grade gliomas(Diagram 28,Table20), but this observation was not significant enough to associate high grade gliomas with complications.

(19) High grade Astrocytoma and condition at discharge

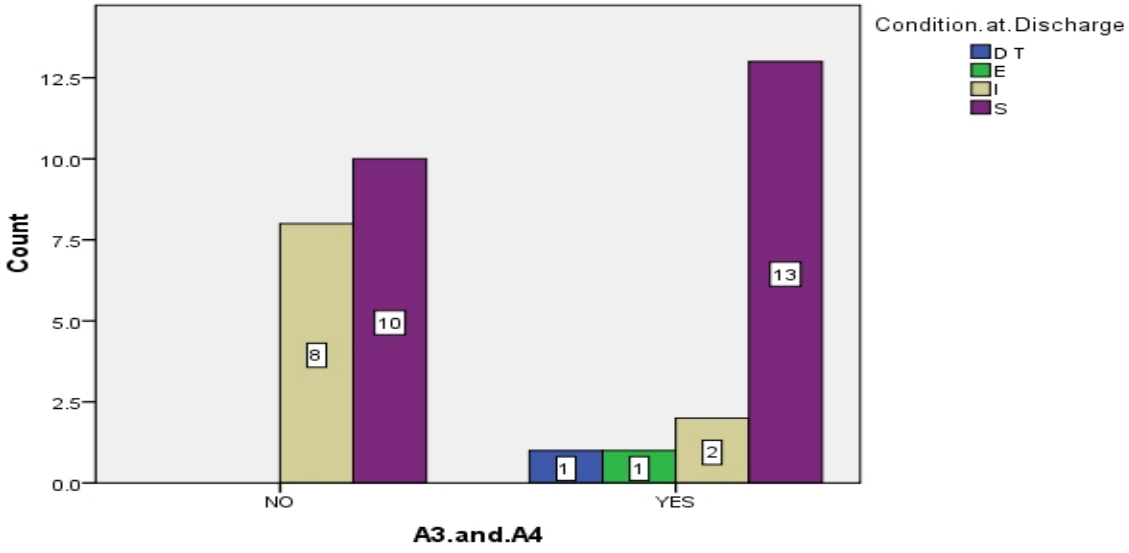


Diagram 29 : High grade astrocytoma and Condition at Discharge

High grade Gliomas and Condition.at.Discharge					
A3.and. A4	D T	E	I	S	Total
NO	0	0	8	10	18
YES	1	1	2	13	17
Total	1	1	10	23	35

High grade Gliomas and Condition.at.Discharge					
A3.and. A4	D T	E	I	S	Total
NO	0	0	8	10	18
YES	1	1	2	13	17
Total	1	1	10	23	35
	2.9%	2.9%	28.6%	65.7%	100.0%

Table 21 : High grade astrocytomas and condition at discharge

Both patients who had adverse post operative events harboured high grade gliomas(Diagram 29,Table21). But this finding also was not significant enough to associate high grade gliomas with adverse post operative events.

(20) Side and diagnosis

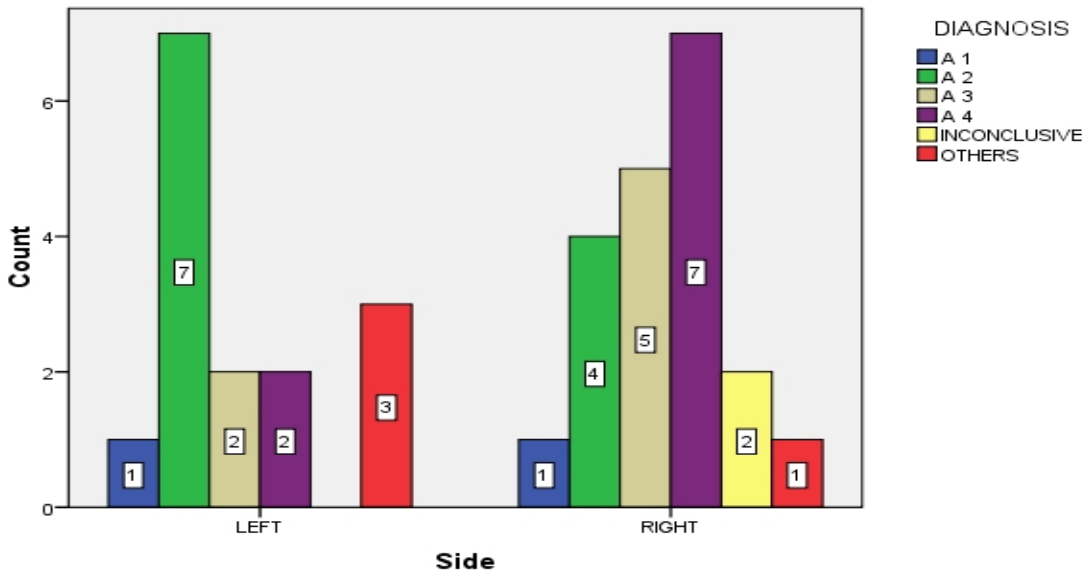


Diagram 30 : Side and diagnosis

DIAGNOSIS							
Side	A 1	A 2	A 3	A 4	INCONCLUSIVE	OTHERS	Total
LEFT	1	7	2	2	0	3	15
RIGHT	1	4	5	7	2	1	20
	2	11	7	9	2	4	35

Table 22 : Side and Diagnosis

Right side lesions had a tendency to have more high grade gliomas 12/16(Diagram 30,Table22) but this was also not significant to associate side with higher grade of gliomas.

(21) Side and location

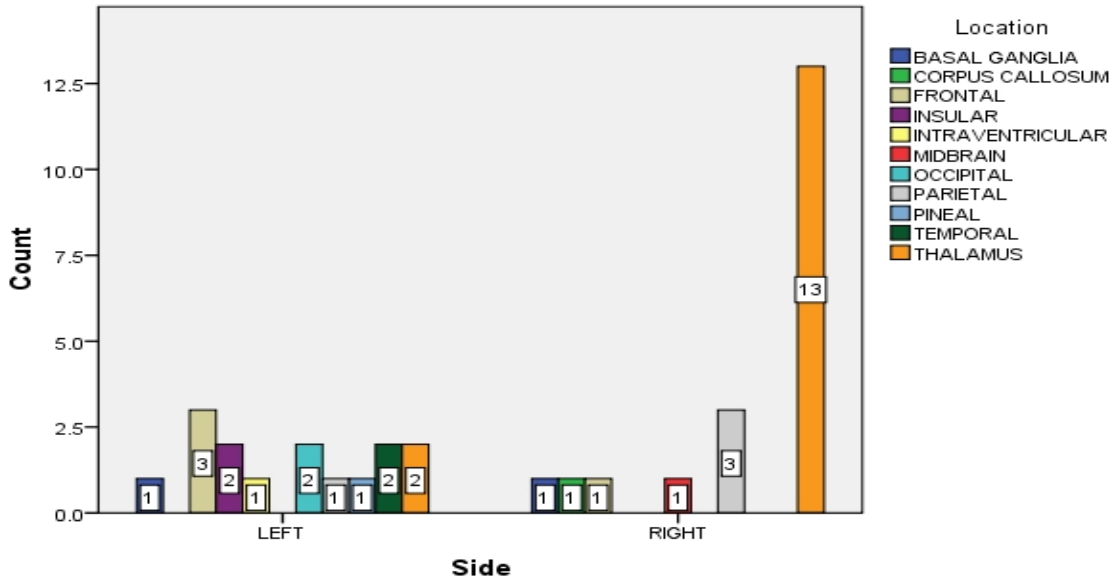


Diagram 31 : Side and Site of Lesion

Location												
Side	BASAL GANGLIA	CORPUS CALLOSUM	FRONTAL	INSULAR	INTRAVENTRICULAR	MIDBRAIN	OCCIPITAL	PARIETAL	PINEAL	TEMPORAL	THALAMUS	Total
LEFT	1	0	3	2	1	0	2	1	1	2	2	15
RIGHT	1	1	1	0	0	1	0	3	0	0	13	20
	2	1	4	2	1	1	2	4	1	2	15	35

Table 23: Comparison of side and site

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	19.756[a]	10	.032
Likelihood Ratio	24.253	10	.007
N of Valid Cases	35		
a. 20 cells (90.9%) have expected count less than 5. The minimum expected count is .43.			

Table 24: Statistical analysis showing significance side and sits.

It was observed in this study that thalamic lesions had a propensity towards right side and lobar lesions had a tendency for left side(Diagram 31,Table23). This was observed to have statistical significance (p = 0.032) (Table24).

(22) Side and complication

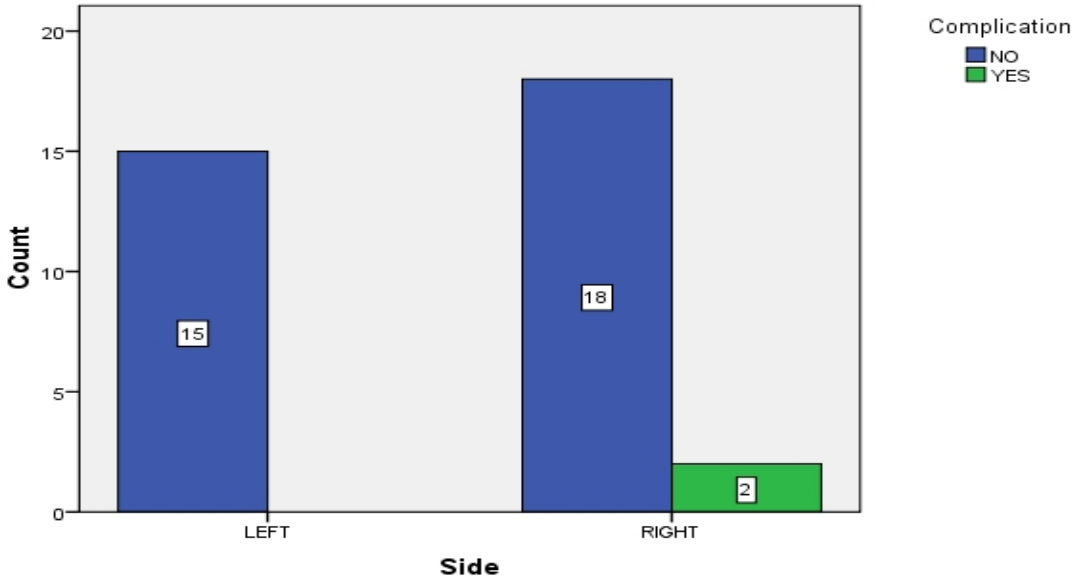


Diagram 32: Side and Complication

	Complication		
Side	NO	YES	Total
LEFT	15	0	15
RIGHT	18	2	20
Total	33	2	35

Table 25 : Side and complication

Both the cases who had postprocedural complications had right sided lesions. But this was not found to be significant(Diagram 32,Table25).

(23) Side and condition at discharge

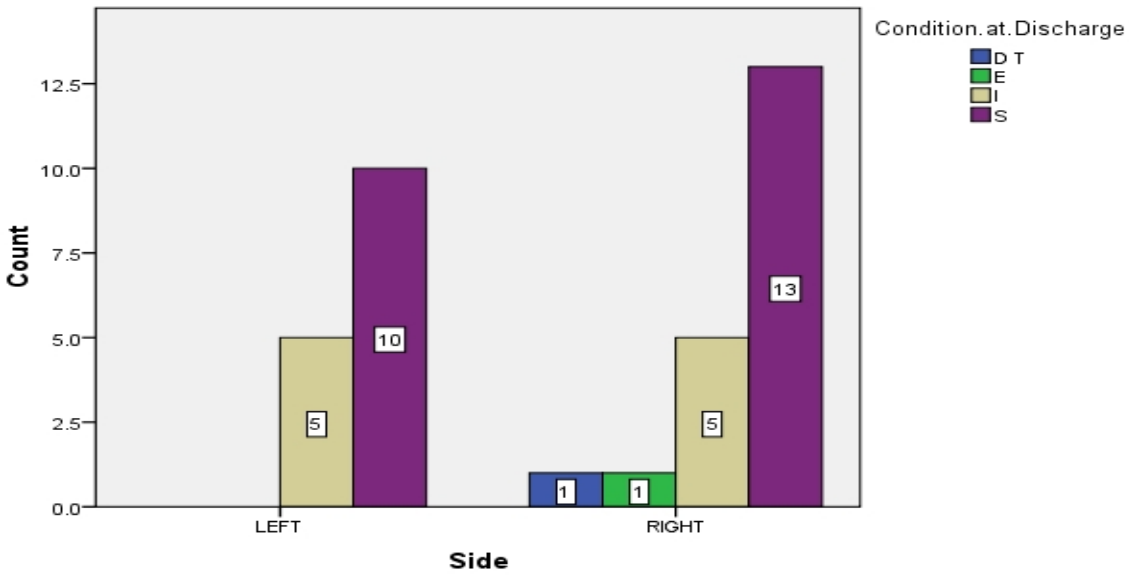


Diagram 33 : Side and condition at discharge

Condition.at.Discharge					
Side	D T	E	I	S	Total
LEFT	0	0	5	10	15
RIGHT	1	1	5	13	20
Total	1	1	10	23	35

Table 26 : Side and Condition at Discharge

Both the cases with adverse postprocedural events(neurological deterioration and death) had right sided lesions(Diagram 33,Table26). But this was not found to be significant.

(24)Diagnosis and location

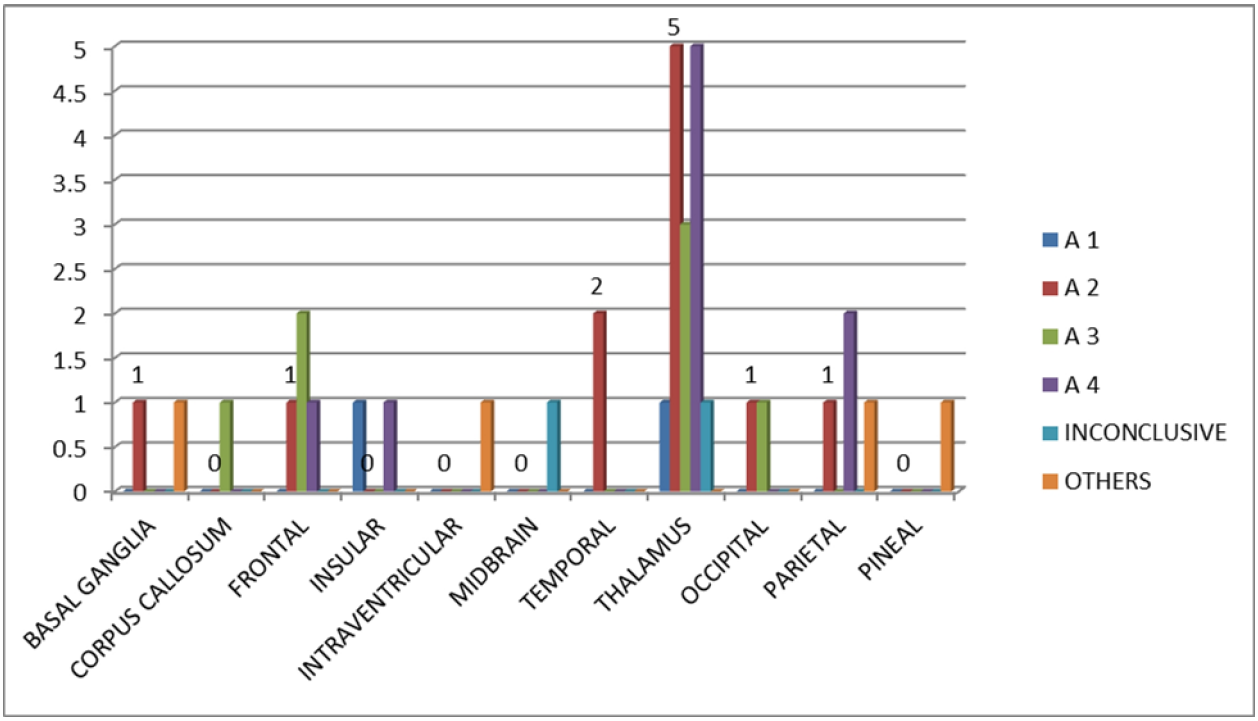


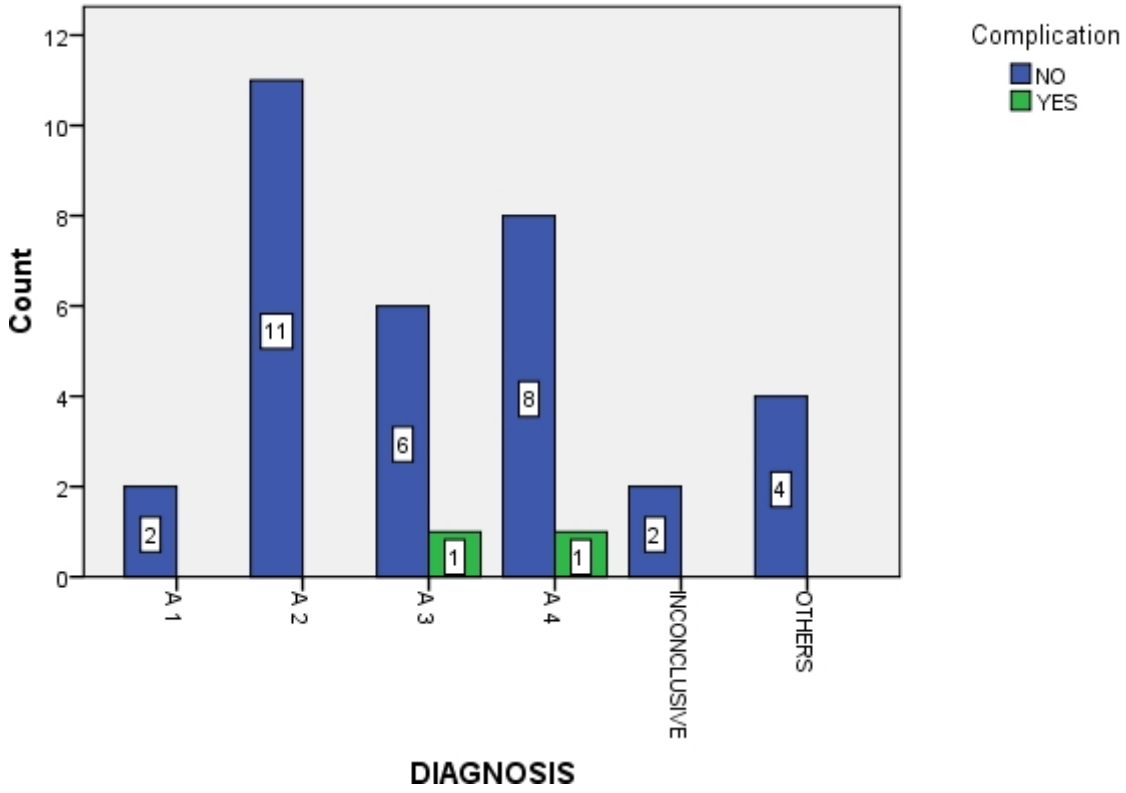
Diagram 34: Diagnosis and location

Astrocytomas were distributed evenly among all sites, both deep and superficial. The one case of germinoma in this study was located in pineal region and ependymoma in intraventricular region. Metastasis from lung was observed to be in the parietal region, and an abscess in gangliocapsular region(Diagram 34).

Donald A Ross[41] in their study comparing STB of brain and thoracoscopic and bronchoscopic biopsy from lung in patients presenting with simultaneous lung lesion and secondaries in brain, observed that the diagnostic yield was 44 – 88%, 74 – 96%, and 90.6 – 99.3% respectively for transthoracic, bronchoscopic ans stereotactic biopsies. The morbidity ranged from 0.6% to 4.8% with death

from 0% to 1.5%. STB was observed to have higher complication rates but the inclusion of diagnoses other than metastatic lung diseases also in the series might have accounted for the increased mortality. The conclusion was STB was a better option when both primary and secondaries of carcinoma lung presented simultaneously.

(25)Diagnosis and complication

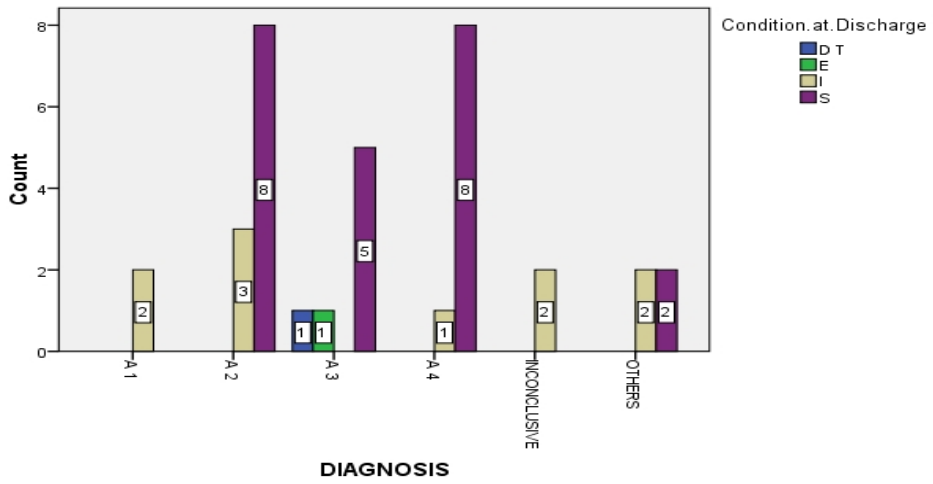


(26) Diagram 35 : Diagnosis and Complications

Astrocytomas were observed to have postprocedural complication but not sufficient enough to get associated with adverse clinical events(Diagram 35).

(26)Diagnosis and condition at discharge

Diagram 36 : showing condition at discharge



33 out of 35 cases studied had uneventful recovery and discharge. The 2 patients who had adverse post operative events harbored astrocytomas(Diagram 36). This finding neared statistical significance (p = 0.09).

ANALYSIS AND DISCUSSION

ANALYSIS AND DISCUSSION

The statistically significant findings were age and diagnosis, age and anesthesia, location and astrocytoma and location and side.

Pathology of a lesion was observed to be influenced by the age of the patient. Grade I astrocytomas were noted exclusively in children, and the grade of astrocytoma increased with increasing age. Certain tumors also had a propensity to involve children of younger age like germinoma and ependymoma.

The choice of anesthesia was influenced by age. Children and elderly were preferentially administered general anesthesia. The choice of general anesthesia in elderly may be due to the fact that most of high grade gliomas were observed in elderly and caused poor neurological and performance status. In anxious children, general anesthesia was safer and a comfort to the surgical team to operate.

Astrocytomas were noted to have preference for thalamus region and hemispherical region. Germinoma was seen in pineal region and ependymoma in intraventricular region. These findings suggested that location influenced the diagnosis and was associated with the diagnosis.

Most of the thalamic lesions were right sided and most of the hemispherical lesions were left sided.

Hemorrhagic complications occurred in patients with high grade astrocytomas and in thalamus only. But this did not rise to statistically significant levels to

conclude that location and grade of gliomas influenced the outcome of the patient. The hemorrhagic complications did not alter the course in the hospital or the condition at discharge.

Another finding observed was the fact that both the inconclusive biopsies were from deep seated lesions. But on statistical analysis this finding was not significant enough to establish an association between negative biopsies and deep-seated lesions.

Deep seated lesions tend to present early because of rapid involvement of vital structures and likely to be smaller in size during their presentation. Thus the location and size greatly influence the yield of biopsy. A larger sample size might have established this relationship beyond doubt.

High grade gliomas are highly vascular lesions and harbor endothelial proliferative changes. The tumor vessels are also devoid of a clear organization and have propensity to bleed. Penetration of the periphery of this tumor with a sharp needle is likely to cause bleeding. Other factors influencing bleeding are a necrotic center and a large tumor volume.

Deep seated lesions also have a tendency to bleed. The longer trajectory of the needle track to reach deeper lesions and the vascularity of deeper structures might be some of the reasons for the increased bleeding rate in deep–seated lesions.

CONCLUSION

CONCLUSION

- Stereotactic biopsy is a safe method for taking samples for biopsy both from superficial and deep seated lesions. It is simple and easy to perform even under local anesthesia.
- The complications associated with this method are minimal and patients will have a good outcome.
- Frameless stereotactic biopsy is a newer model and method, performs well, and appropriate in technology.
- STB is a good alternative in neurosurgical procedures.

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BIBLIOGRAPHY

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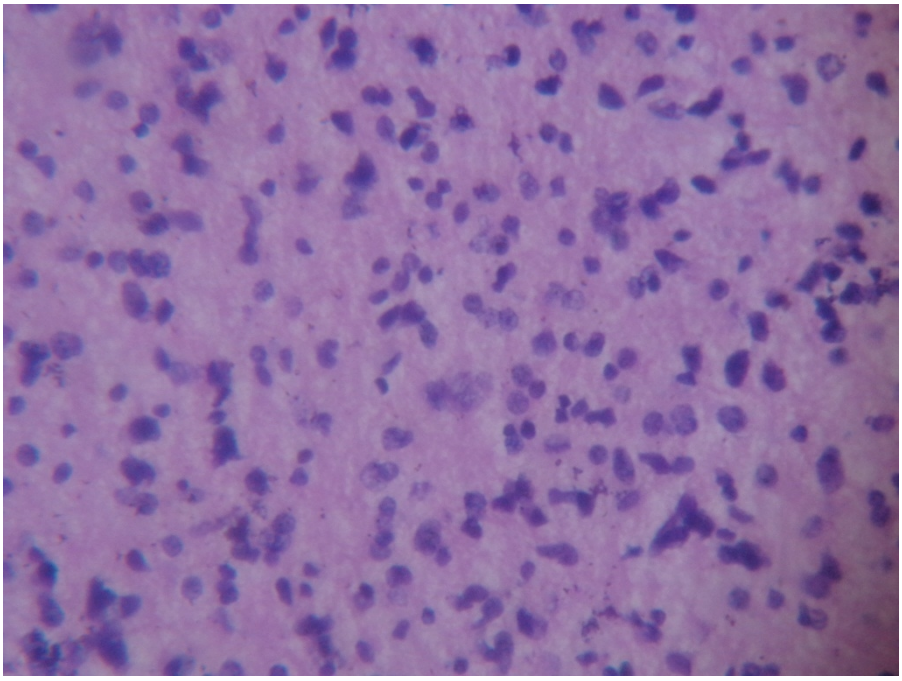
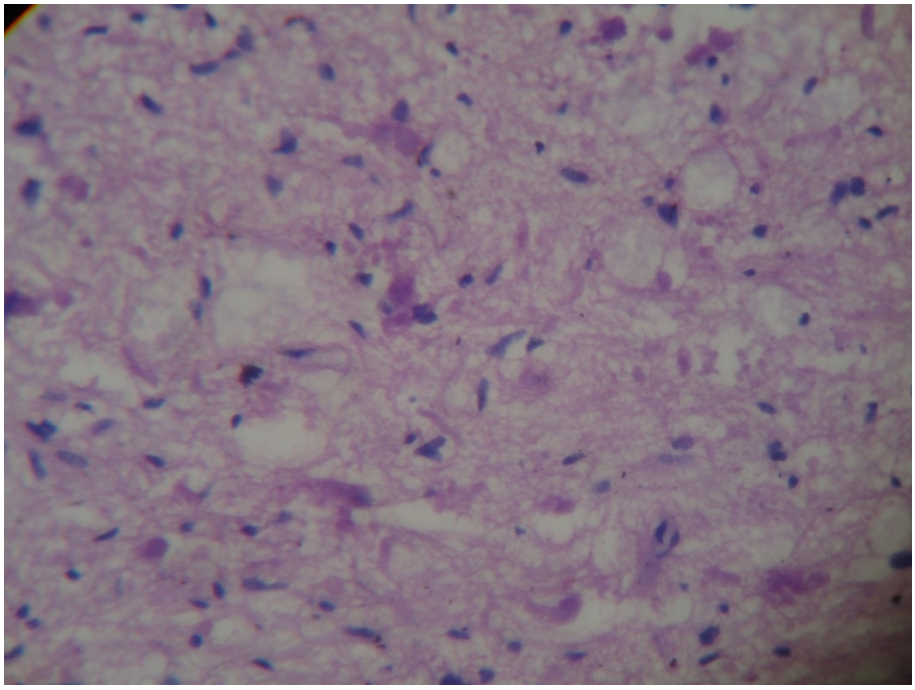
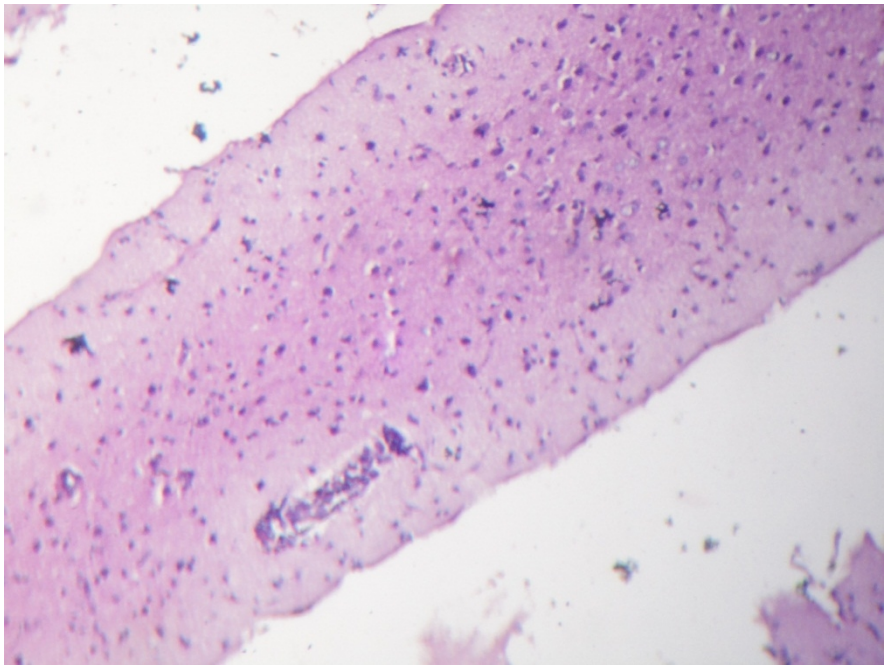


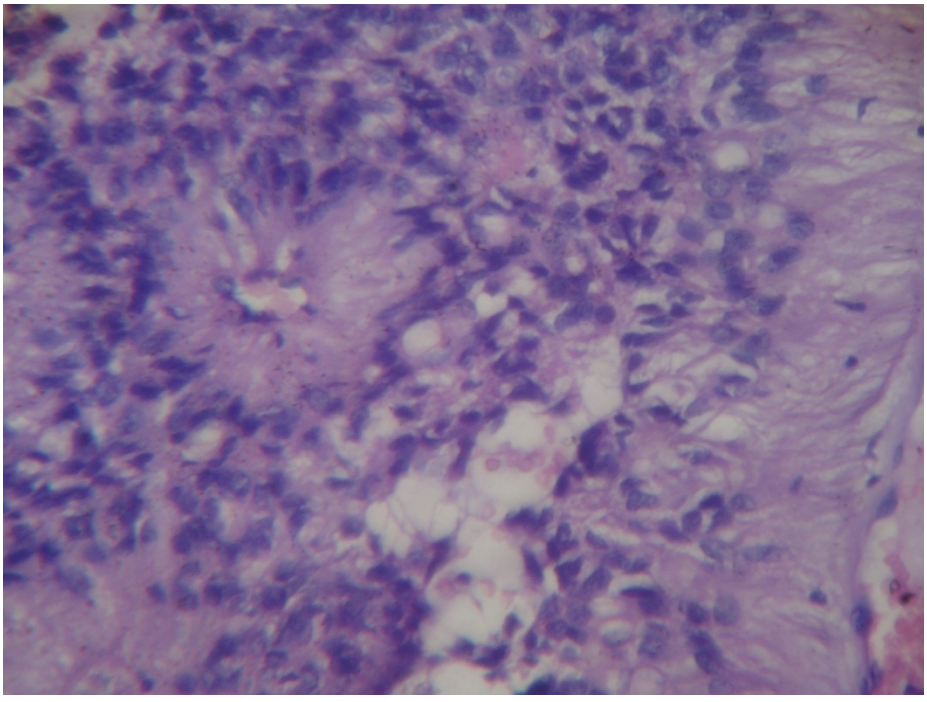
Color Plate 1: Section shows regions of dense cellularity, nuclear pleomorphism, and gemistocytes.
(patient 11: A case of Anaplastic astrocytoma – Thalamus)



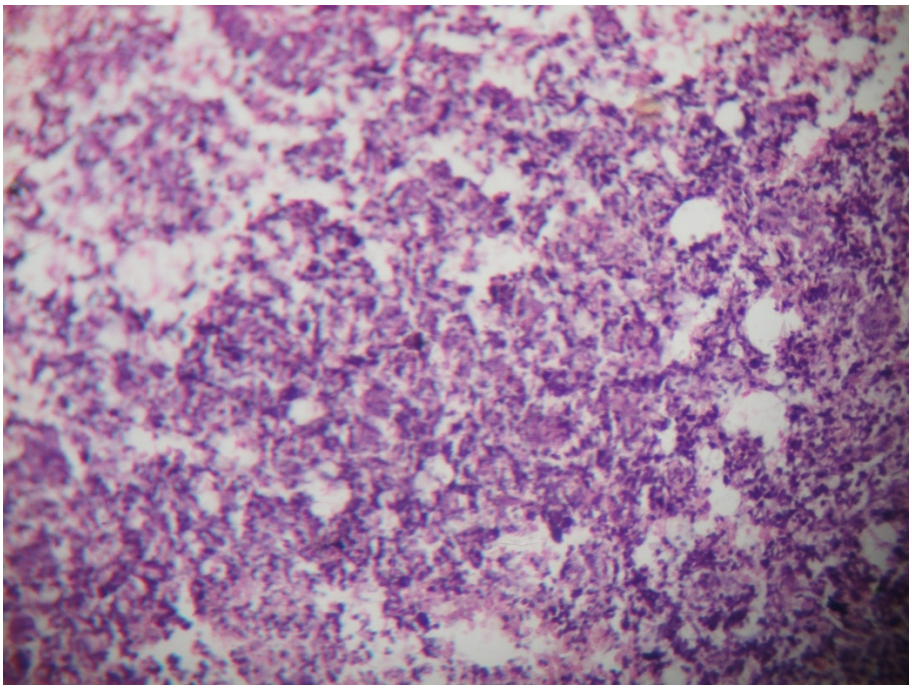
Color Plate 2: Section shows low cellularity with piloid processes, and eosinophilic granular bodies.
This is a case of pilocytic astrocytoma. (patient 24).



Color Plate 3: section shows sparse cellularity with uniform nuclei suggestive of low grade glioma.
(Patient 15: A case of low grade gliomas thalamus)



Color Plate 4: Section shows ependymal cells with perivascular pseudorossettes.
(Patient 23: a case of classical ependymoma Gr II, Left lateral interventricular region)



Color Plate 5: Section shows region of dense cellularity with uniform small cells and scant cytoplasm with foci of necrosis.
(Patient 9: A case of secondaries brain with lesion seen in right lung on CT chest – brain secondaries from lung)

APPENDIX I - Ethical Committee Approval

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To

Dr.S.Siva Subramanyam,,
Post Graduate in Neurosurgery,
Madras Medical College, Chennai -3

Dear Dr.S.Siva Subramanyam,

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "A prospective Analytical study on CT guided frameless stereotactic Biopsy" No.10122012.

The following members of Ethics Committee were present in the meeting held on 11.12.2012 conducted at Madras Medical College, Chennai -3.

1.	Dr.S.K.Rajan, M.D.FRCP, DSc	--- Chairperson
2.	Prof. R. Nandhini MD Director, Instt. of Pharmacology ,MMC, Ch-3	-- Member Secretary
3.	Prof. Dr.A.Radhakrishnan MD Director , Inst. Of Internal Medicine, MMC, Ch-3	-- Member
4.	Prof. Meenalochani, MD Director , Instt. of O& G, Chennai	-- Member
5.	Prof. Shyamraj MD Director i/c , Instt. of Biochemistry , MMC, Ch-3	-- Member
6.	Prof. P. Karkuzhali. MD Prof., Instt. of Pathology, MMC, Ch-3	-- Member
7.	Prof. S.Devivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
8.	Thiru. S. Govindsamy. BA, BL	-- Lawyer
9.	Tmt.Arnold Saulina MA MSW	--- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

R Nandini 21/12/12
Member Secretary, Ethics Committee

APPENDIX II - Copy of Informed Consent ஆராய்ச்சி ஒப்புதல் கடிதம

ஆராய்ச்சி தலைப்பு : "A PROSPECTIVE ANALYTICAL STUDY ON CT GUIDED FRAMELESS STEREOTACTIC BRAIN BIOPSY" பற்றிய ஆய்வு

பெயர் : வயது/பால் : **தேதி :**

ஆராய்ச்சி சேர்க்கை எண் :

ராஜீவ் காந்தி அரசு மருத்துவக்கல்லூரி மற்றும் அரசு பொது மருத்துவமனையின் நரம்பியல் அறுவை சிகிச்சைத் துறையில் "A PROSPECTIVE ANALYTICAL STUDY ON CT GUIDED FRAMELESS STEREOTACTIC BRAIN BIOPSY" பற்றிய ஆய்வு நடைபெறுகிறது என்பதை அறிந்து கொண்டேன்

- சிடி ஸ்கே , மற்றும் எம்.ஆர்.ஐ ஸ்கேன் ஆகியவற்றின் அடிப்படையில் இந்த ஆய்வு டைபெறுகிறது என்பதையும் மேலும் அறுவை சிகிச்சையின் நேரடியாக பார்க்கப்படுவதை வைத்தும் ஆய்வு நடைபெறுகிறது என்ப அறிந்து கொண்டேன்
- இவ்வாய்வில் கலந்து கொள்பவர்களின் சொந்த தகவல்கள் பாதுக்காகபடும் என்பதையும் இந்த ஆய்வின் முடிவுகளை பிரசுரிக்கு அல்லது வெளியிடும்போதோ தங்களின் எனது தகவல்கள் ஏதும் வெளியிடபடாத என்பதையும் அறிந்து கொண்டேன்
- இந்த ஆராய்ச்சியிலிருந்து எந்த நேரமும் பின் வாங்கலாம் என்றும், அதனால் எந்த பாதிப்பும் எற்படாது என்பதையும் அறிந்து கொண்டே
- இந்த ஆய்வில் பங்குபெற அல்லது விலகிக்கொள்ள எனக்கு முழு சுதந்திரம் உண்டு என்பதையு , இந்த ஆய்வில் இருந்து நான் விலகிகொண்டாலு கிடைக்கவேண்டிய சிகிச்சை தொடர்ந்து கிடைக்கும் என்பதையும் கொண்டேன்
- இந்த ஆராய்ச்சியின் விவரங்களு , அதன் நோக்கங்களும் எனக்கு தெளிவ விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விவரங்களை புரிந்து கொண்டு, இந்த ஆய்வில் கலந்து கொள்ள சம்மதிக்கிறே
- இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் தான் பங்கு பெறுகிறேன்

கையொப்பம்

APPENDIX III - Copy of Patient Information Sheet

ஆராய்ச்சித் தகவல் த

- தங்களின் சிடி ஸ்கேன் / எம்.ஆர்.ஐ ஸ்கேன் படம் அல்லத நகல் அல்லது படத்தின் நிழல்படம் இங்கு பெறப்பட்டுள்
- அரசு மருத்துவக்கல்லூரி மற்றுப் மருத்துவமனையின் நரம்பியல் அறுவை சிகிச்சைத் துறையில்

"A **PROSPECTIVE ANALYTICAL STUDY ON CT GUIDED FRAMELESS STEREOTACTIC BRAIN BIOPSY**" பற்றிய ஆய்வு நடைபெறுகிற

- சிடி ஸ் , மற்றும் எம்.ஆர்.ஐ ஸ்கேன் ஆகிய அடிப்படையில் இந்த ஆய்வு நடைபெறுகிற
- இவ்வாய்வில் கலந்து கொள்பவர்களின் சொந்த த ரகசியமாக பாதுக்காகபடும்
- இந்த ஆய்வின் வுகளை பிரசுரிக்குபோது வெளியிடும்போதோ தங்களின் சொந்த தகவல்கள் வெளியிடபடாது
- இந்த ஆய்வில் பங்குபெற அல்லது விலகிக்கொள்ள முழு சுதந்திரம் உண்
- இந்த ஆய்வில் இருந்து நீங்கள் விலகிகொண்டாலும் உங் கிடைக்கவேண்டிய சிகிச்சை தொடர்ந்து கிடைக்கும்

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள்

APPENDIX IV - COPY OF PROFORMA USED

Serial No:

Name: Age: MIN No: I.P. No:

Sex: M / F

Complaints

History of Presenting Illness

Past History

History of Hypertension – Years – Control
-Treatment: :

History of Smoking- Years :

History of Alcoholism- Years :

Examination

Consciousness, orientation, any deficits in higher mental functions:
Glasgow coma scale :
Any cranial nerve dysfunction :
Cranial nerve examination :
Pupils :
Any neurological deficit :
Any other system disorder :
Pulse : /min

Investigations

CT brain :

MRI Brain : Location, size, relationship to ventricles, T1, T2, Diffusion Weighted characters, Enhancement, relationship to vessels

Management

Surgery done :
Anesthesia :
Frame used :
Intraoperative complication if any:
Time to complete the procedure :
Depth from surface:
Number of passes made to take biopsy:
Material aspirated:
Site of burr hole :

Postoperative period:
Time to recovery:
Any new deficit:
Post-operative CT:

Edema :
Bleed :
Breach of ventricle :
Any new changes:

Biopsy :

Report

APPENDIX V –MASTER CHART

Name	Age	Sex	HPE no	Diagnosis	Diagnosis	Location	Side	Type of anesthesia	Complicatio n	Condition at discharge or	Recovery	Infection	Site	Surgical Time	Followup
PATIENT 1	62	M	527/10	A 4	Glioblastoma	THALAMUS	R	I	n	I	uneventful	n	medial	20	RT
PATIENT 2	45	M	-------	O	Brain abscess	BASAL GANGLIA	R	I	n	S	uneventful	n	medial	25	Aspiration
PATIENT 3	45	F	8\11	A 2	Astrocytoma grade 2	FRONTAL	L	I	n	S	uneventful	n	lateral	25	Follow up
PATIENT 4	11	M	21/11	O	Germinoma	PINEAL	L	g	n	I	uneventful	n	medial	30	RT
PATIENT 5	30	F	86/11	A 2	Astrocytoma grade 2	BASAL GANGLIA	L	I	n	I	uneventful	n	medial	20	RT
PATIENT 6	21	M	216/11	A 2	Astrocytoma grade 2	THALAMUS	L	g	n	S	uneventful	n	medial	25	RT
PATIENT 7	13	F	243/11	A 2	Astrocytoma grade 2	THALAMUS	R	g	n	S	uneventful	n	medial	30	RT
PATIENT 8	48	M	262/11	A 3	astrocytoma grade 3	CORPUS CALLOSUM	R	I	n	S	uneventful	n	medial	25	RT
PATIENT 9	45	M	276/11	O	Secondaries lung	PARIETAL	L	I	n	I	uneventful	n	middle	25	CCT
PATIENT 10	45	M	320/11	IN	Inconclusive	THALAMUS	R	I	n	I	uneventful	n	lateral	25	Surgery
PATIENT 11	49	M	478/11	A 3	astrocytoma grade 3	THALAMUS	R	g	n	S	uneventful	n	medial	35	RT
PATIENT 12	67	F	527/11	A 3	astrocytoma grade 3	THALAMUS	R	g	H	TD	uneventful	n	medial	30	RT
PATIENT 13	28	F	534/11	A 2	Astrocytoma grade 2	THALAMUS	L	I	n	S	uneventful	n	medial	25	RT
PATIENT 14	68	M	540/11	A 3	astrocytoma grade 3	FRONTAL	L	g	n	S	uneventful	n	middle	20	RT
PATIENT 15	24	F	593/11	A 2	Astrocytoma grade 2	THALAMUS	R	I	n	S	uneventful	n	medial	20	RT
PATIENT 16	45	M	39/12	A 4	Glioblastoma	THALAMUS	R	I	H	S	uneventful	n	medial	30	RT
PATIENT 17	60	F	63/12	A 4	Glioblastoma	PARIETAL	R	I	n	S	uneventful	n	middle	30	RT
PATIENT 18	42	M	72/12	A 2	Astrocytoma grade 2	OCCIPITAL	L	I	n	S	uneventful	n	lateral	30	Follow up
PATIENT 19	25	M	168/12	A 3	astrocytoma grade 3	OCCIPITAL	L	I	n	S	uneventful	n	lateral	25	RT
PATIENT 20	55	F	234/12	A 2	Astrocytoma grade 2	TEMPORAL	L	I	n	S	uneventful	n	lateral	25	RT
PATIENT 21	46	F	250/12	A 2	Astrocytoma grade 2	TEMPORAL	L	I	n	I	uneventful	n	lateral	35	Follow up
PATIENT 22	30	M	279/12	A 4	Glioblastoma	THALAMUS	R	I	n	S	uneventful	n	medial	25	RT

PATIENT 23	24	F	284/12	O	Classical ependymoma	INTRAVENTRICULAR	L	I	n	S	uneventful	n	medial	30	RT
PATIENT 24	11	M	297/12	A 1	astrocytoma Grade 1	INSULAR	L	g	n	I	uneventful	n	middle	20	Surgery
PATIENT 25	58	F	330/12	A 4	Glioblastoma	INSULAR	L	I	n	S	uneventful	n	middle	25	RT
PATIENT 26	60	M	379/12	A 4	Glioblastoma	PARIETAL	R	I	n	S	uneventful	n	middle	25	RT
PATIENT 27	38	M	387/12	A 4	Glioblastoma	THALAMUS	R	g	n	S	uneventful	n	middle	30	RT
PATIENT 28	52	M	405/12	A 4	Glioblastoma	THALAMUS	R	g	n	S	uneventful	n	medial	30	RT
PATIENT 29	49	F	428/12	IN	Inconclusive	MIDBRAIN	R	I	n	I	uneventful	n	medial	25	Advised surgery but patient refused
PATIENT 30	51	M	582/12	A 4	Glioblastoma	FRONTAL	L	g	n	S	uneventful	n	lateral	20	RT
PATIENT 31	36	M	584/12	A 2	Astrocytoma grade 2	PARIETAL	R	I	n	I	uneventful	n	lateral	30	Follow up
PATIENT 32	35	M	31/13	A 2	Astrocytoma grade 2	THALAMUS	R	I	n	S	uneventful	n	medial	25	RT
PATIENT 33	27	F	44/13	A 3	astrocytoma grade 3	THALAMUS	R	g	n	E	uneventful	n	medial	30	RT
PATIENT34	37	M	94/13	A 3	astrocytoma grade 3	FRONTAL	R	I	n	S	uneventful	n	lateral	25	RT
PATIENT 35	8	M	120/13	A 1	astrocytoma Grade 1	THALAMUS	R	g	n	I	uneventful	n	middle	25	Surgery

APPENDIX VI – TURNITIN REPORT FOR PLAGIARISM

A PROSPECTIVE ANALYTICAL STUDY ON CT GUIDED FRAMELESS STEREOTACTIC BRAIN BIOPSY by Sivasubramanyam Selvaraj 16101509 M.Ch. Neuro Surgery

From Medical (TNMGRMU APRIL 2013 EXAMINATIONS)

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Serge Goldman, "Brain Tumors", Methods in Molecular Biology, 2011

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